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=> b reg
FILE 'REGISTRY' ENTERED AT 10:08:59 ON 04 MAY 2004
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STRUCTURE FILE UPDATES:
                           2 MAY 2004
                                       HIGHEST RN 678693-82-8
DICTIONARY FILE UPDATES:
                           2 MAY 2004
                                       HIGHEST RN 678693-82-8
TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004
  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.
Crossover limits have been increased. See HELP CROSSOVER for details.
Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html
=> d que 19
              1 SEA FILE=REGISTRY ABB=ON PLU=ON 142880-36-2/RN
T.9
=> d ide 19
     ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
1.9
     142880-36-2 REGISTRY.
RN
     Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-
     2-oxoethyl]-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
     Butanediamide, N4-hydroxy-N1-[1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-
     oxoethyl]-2-(2-methylpropyl)-, [S-(R^*,S^*)]-
OTHER NAMES:
     CS 610
CN
     Galardin
     GM 6001
    Ilomastat
     STEREOSEARCH
     C20 H28 N4 O4
MF
SR
LC
                  ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CA, CANCERLIT,
```

Absolute stereochemistry.

Other Sources:

USAN, USPATZ, USPATFULL

WHO

CAPLUS, CASREACT, CHEMCATS, CIN, DDFU, DRUGU, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, MEDLINE, PHAR, PROMT, SYNTHLINE, TOXCENTER,

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

- 80 REFERENCES IN FILE CA (1907 TO DATE)
- 3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
- 82 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> d que 110

L10

1 SEA FILE=REGISTRY ABB=ON PLU=ON 421553-77-7/RN

=> d ide 110

L10 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN

421553-77-7 REGISTRY

Butanediamide, N1-[(1S)-2-[(2-aminoethyl)amino]-1-methyl-2-oxoethyl]-N4hydroxy-2-(2-methylpropyl)- (9CI) (CA INDEX NAME) OTHER NAMES:

CN IC 3

FS STEREOSEARCH

MF C13 H26 N4 O4

SR CA

LCSTN Files:

CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

- 1 REFERENCES IN FILE CA (1907 TO DATE)
- 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> b home FILE 'HOME' ENTERED AT 10:09:38 ON 04 MAY 2004

=>

=> b reg FILE 'REGISTRY' ENTERED AT 09:55:27 ON 04 MAY 2004 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2004 American Chemical Society (ACS)

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STRUCTURE FILE UPDATES: 2 MAY 2004 HIGHEST RN 678693-82-8 DICTIONARY FILE UPDATES: 2 MAY 2004 HIGHEST RN 678693-82-8

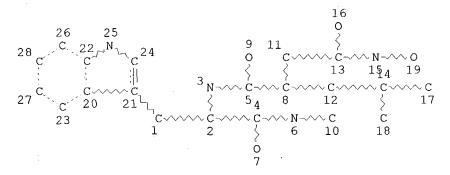
TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at: http://www.cas.org/ONLINE/DBSS/registryss.html

=> d que 117 L13 STR



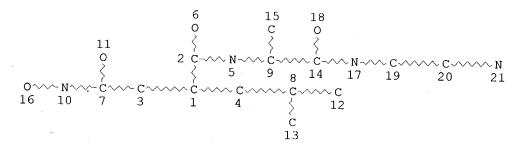
NODE ATTRIBUTES: DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES: RING(S) ARE ISOLATED OR EMBEDDED NUMBER OF NODES IS 28

STEREO ATTRIBUTES: NONE

L17 120 SEA FILE=REGISTRY SSS FUL L13

=> d que 118 L15 STR



NODE ATTRIBUTES: DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES: RING(S) ARE ISOLATED OR EMBEDDED NUMBER OF NODES IS 21

STEREO ATTRIBUTES: NONE L18 178 SEA FILE=REGISTRY SSS FUL L15

≃>

=> b hcaplus FILE 'HCAPLUS' ENTERED AT 10:02:20 ON 04 MAY 2004 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

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FILE COVERS 1907 - 4 May 2004 VOL 140 ISS 19 FILE LAST UPDATED: 3 May 2004 (20040503/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

=> d que 120 nos L13 STR L15 STR 120 SEA FILE=REGISTRY SSS FUL L13 L17 178 SEA FILE=REGISTRY SSS FUL L15 L18 L19 142 SEA FILE=HCAPLUS ABB=ON PLU=ON L17 OR L18 63 SEA FILE=HCAPLUS ABB=ON PLU=ON L19 AND P/DT L20

=> d ibib abs hitstr 120 1-63

L20 ANSWER 1 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

2004:310824 HCAPLUS

TITLE:

Compounds and methods for the modulation of CD154 for preventing thrombosis and coagulation and reducing

activation of cells in inflammatory response

INVENTOR(S):

Phillips, David; Yan, Yibing; Alaimo, Lisa; Prasad,

Srinivasa

PATENT ASSIGNEE(S):

IISA

SOURCE:

U.S. Pat. Appl. Publ., 41 pp., Cont.-in-part of U.S.

Pat. Appl. 2004 48,803.

CODEN: USXXCO

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
			~	
US 2004072750	A1	20040415	US 2003-376425	20030228
US 2002165166	A1	20021107	US 2001-2585	20011130
WO 2002089730	A2	20021114	WO 2002-US13900	20020503
WO 2002089730	A 3	20030213		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG A1 20040311 US 2003-368947 20030217 US 2004048803 US 2001-289049P P 20010503 PRIORITY APPLN. INFO.: US 2001-2585 A1 20011130 WO 2002-US13900 A2 20020503 US 2003-368947 A2 20030217

The invention relates to compds. that are capable of modulating CD154 mobilization and that are useful for stabilizing the thrombotic and/or coagulation process and/or reducing the activation of cells involved in an inflammatory response. The invention also relates to methods useful for identifying such compds. The invention also relates to the treatment of platelets for transfusion with metalloproteinase inhibitors to treat or prevent inflammation. The present invention also includes compns. and methods to treat injury and disease related to such biol. processes. GPIID/IIIa inhibition with eptifibatide lowered levels of sCD40L and RANTES post stenting, conferring antiinflammatory as well as antithrombotic effects.

IT INDEXING IN PROGRESS

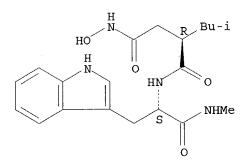
IT 142880-36-2, GM6001

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (metalloproteinase inhibitor, soluble CD154 release inhibition by; CD154 modulator for prevention of thrombosis, coagulation, and inflammatory response)

RN 142880-36-2 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L20 ANSWER 2 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

2004:252305 HCAPLUS

DOCUMENT NUMBER:

140:281409

TITLE:

Inhibition or activation of ADAM9 and ADAM15 for

treatment of vascularization-related disease and wound

healing

INVENTOR (S):

Blobel, Carl P.; Horiuchi, Keisuke; Weskamp, Gisela;

Preissner, Klaus

PATENT ASSIGNEE(S):

Sloan-Kettering Institute for Cancer Research, USA;

University of Mannheim/heidelberg;

Justus-Liebig-Universitaet Giessen; Hammes, Hans-Peter

PCT Int. Appl., 32 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

SOURCE:

Patent English

LANGUAGE: FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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PATENT NO.
                                              KIND DATE
                                                                                                       APPLICATION NO. DATE
                                                                                                       WO 2003-US28751 20030911
WO 2004024089
                                                A2
                                                               20040325
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU
          RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
                      GW, ML, MR, NE, SN, TD, TG
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PRIORITY APPLN. INFO.:

US 2002-409858P P 20020911

Inhibition of neovascularization is achieved by exposing a tissue susceptible to neovascularization to a therapeutic agent effective to inhibit ADAM9 and/or ADAM15. The therapeutic agent may be, for example, an antibody, a small mol. therapeutic, an antisense or RNAi therapeutic, or an agent for introducing targeted mutations in the genetic sequence for ADAM9 and/or ADAM15. Thus, an individual suffering from a condition associated with pathol. neovascularization is treated by administration of a therapeutic agent effective to inhibit an ADAM9 or ADAM15. Activation of ADAM9 or ADAM15 can be used for promotion of neovascularization, for example to facilitate wound healing, perfusion or circulation. In this case, the therapeutic agent used is one which enhances the active amount of ADAM9 and/or ADAM15. Inhibition or activation of ADAM9 and/or ADAM15 in accordance with the methods of the invention provides an attractive alternative to targeting of other ADAM species, such as ADAM10, because neither ADAM9 nor ADAM15 appears to be essential for development or maintenance. Thus, side effects are minimized. The growth of B16F10 melanoma tumors was reduced in ADAM9-/- and ADAM15-/- mice compared to wild-type mice.

IT 143457-40-3, TAPI

> RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (ADAM9 or ADAM15 inhibitor; ADAM9 and ADAM15 inhibition or activation

for treatment of vascularization-related disease and wound healing)

RN143457-40-3 HCAPLUS

L-Alaninamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-3-CN (2-naphthalenyl)-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L20 ANSWER 3 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

2004:203542 HCAPLUS

DOCUMENT NUMBER:

140:247105

TITLE:

Metalloproteinase inhibitor compounds and methods for the modulation of CD154, and use for stabilizing the thrombotic and/or coagulation process and/or reducing the activation of cells involved in an inflammatory

response

INVENTOR (S):

Phillips, David; Andre, Patrick

PATENT ASSIGNEE(S):

SOURCE:

U.S. Pat. Appl. Publ., 41 pp., Cont.-in-part of Appl.

No. PCT/US2002/13900.

CODEN: USXXCO

DOCUMENT TYPE:

LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT 1	NO.	KIND			APPLICATION NO.				Ο.	DATE				
US 2004	048803	A 1	2004	0311		Ü	S 20	03-3	6894	7	2003	0217		
US 2002	165166	A 1	2002	1107		U	S 20	01-2	585		2001	1130		
	089730										2002			
	089730							· · ·	0100		2002			
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	CO, CR,	CU, CZ	, DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,
	GM, HR,	HU, II	, IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	KZ,	LC,	LK,	LR,
	LS, LT,	LU, LV	, MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	OM,	PH,
	PL, PT,	RO, RU	, SD,	SE,	SG,	SI,	SK,	SL,	TJ,	TM,	TN.	TR,	TT,	TZ,
	UA, UG,	•												
	TJ, TM	-						-		-				_
RW:	GH, GM,	KE, LS	, MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	ΑT,	ΒE,	CH,
	CY, DE,	DK, ES	, FI,	FR,	GB,	GR,	IE,	IT,	LU,	MC,	NL,	PT,	SE,	TR,
	BF, BJ,	CF, CC	, CI,	CM,	GA,	GN,	GO,	GW,	ML,	MR.	NE,	SN,	TD,	TG
US 2004	072750	Å1	2004	0415	•	U.	S 20	03 <i>-</i> 3'	7642.	5	2003	0228	•	
PRIORITY APP	LN. INFO	. :			1	US 2	001-	2890	49P	P	2001	0503		
					1	US 2	001-	2585		A 1	2001	1130		
											2002			
											2003			
AR The inv	ention r	elates	to co	mnds									יומי	54

AB The invention relates to compds. that are capable of modulating CD154 mobilization and that are useful for stabilizing the thrombotic and/or coagulation process and/or reducing the activation of cells involved in an inflammatory response. Compds. of the invention include metalloproteinase inhibitors. The invention also relates to methods useful for identifying such compds. The invention also relates to the treatment of platelets for

transfusion with metalloproteinase inhibitors to treat or prevent inflammation. The invention also includes compns. and methods to treat injury and disease related to such biol. processes.

IT 142880-36-2, Galardin

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(metalloproteinase inhibitor compds. and methods for modulation of CD154, and use for stabilizing thrombotic and/or coagulation process and/or reducing activation of cells involved in inflammatory response)

RN 142880-36-2 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L20 ANSWER 4 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: DOCUMENT NUMBER:

2003:875135 HCAPLUS 139:333136

TITLE:

Combination therapy using a proteasome/ubiquitination inhibitor and a matrix metalloproteinase inhibitor to

treat a catabolic state and/or cachexia in a patient Strous, Gerardus Jacobus Antonius Maria; Van Kerkhof,

Petrus Johannes Maria

PATENT ASSIGNEE(S):

Universiteit Utrecht Holding B.V., Neth.; UMC Utrecht

Holding B.V.

SOURCE:

PCT Int. Appl., 25 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

INVENTOR(S):

Patent English

LANGUAGE:

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.				KIND DATE				APPLICATION NO. DATE								
								-								
WO 2003	0907	77	Α	1 :	2003	1106		W	20	03-N	L303		2003	0424		
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	CN,	CO,	CR,	CU,	CZ,	CZ,	DE,	DE,	DK,	DK,	DM,	DZ,	EC,	EE,	EE,	ES,
	FΙ,	FΙ,	GB,	GD,	GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KΕ,	KG,
-	ΚP,	KR,	ΚZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,
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	ZM,	ZW,	ΑM,	AZ												
RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	ŪĠ,	ZM,	ZW,	AT,	BE,	BG,
	CH,	CY,	CZ,	DE,	DK,	EE,	ES,	FI,	FR,	GB,	GR,	HU,	ΙE,	IT,	LU,	MC,
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	GW,	ML,	MR,	ΝE,	SN,	TD,	TG									

20031029 EP 2002-76675 20020425 EP 1356819 Α1

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.: EP 2002-76675 Α 20020425 US 2002-375557P P 20020425

The invention relates to the field of proteins, more specifically to AB proteins that are located on the surface of cells. The invention provides a method for upregulating the bioavailability of a cell surface receptor comprising decreasing both the uptake and/or degradation of said receptor and the extracellular cleaving of the receptor. The invention further provides pharmaceutical compns. for upregulating the bioavailability of a growth hormone receptor, comprising a proteasome/ubiquitination inhibitor and a matrix metalloproteinase inhibitor, as well as the use of these pharmaceutical compns. for the manufacture of a medicament for increasing anabolic conditions in human patients suffering from a catabolic state and/or cachexia.

142880-36-2, GM6001 TT

RL: PAC (Pharmacological activity); BIOL (Biological study) (proteasome/ubiquitination inhibitor-matrix metalloproteinase inhibitor combination to treat catabolic state and/or cachexia)

142880-36-2 HCAPLUS RΝ

Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-CN 2-oxoethyl]-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS REFERENCE COUNT: 5 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 5 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

2003:591202 HCAPLUS

DOCUMENT NUMBER:

139:145836

TITLE:

Synthetic peptide substrates of human aggrecanase-1

and -2 for drug screening applications

INVENTOR (S): PATENT ASSIGNEE(S): Fourie, Anne; Karlsson, Lars; Coles, Fawn Ortho McNeil Pharmaceutical, Inc., USA

SOURCE:

PCT Int. Appl., 63 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2003062263	A2	20030731	WO 2003-US1327	20030115
WO 2003062263	А3	20040115		

AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,

ML, MR, NE, SN, TD, TG

US 2003166037 A1 20030904 US 2002-50200 A 20020116 US 2002-50200 PRIORITY APPLN. INFO.:

The present invention describes synthetic peptide substrates of the metalloproteases, agggrecanase-1 and/or -2 suitable for assays of enzyme activity. The substrates are peptides less than 40 amino acids in length having a cleavage site between Glu on the N-terminal side of the cleavage site and a non-polar or uncharged residue on the C-terminal side of the cleavage site. The invention also describes methods using these peptides to discover pharmaceutical agents that modulate these proteases:

IT 163958-74-5

> RL: BSU (Biological study, unclassified); BIOL (Biological study) (aggrecanase inhibition by; synthetic peptide substrates of human aggrecanase-1 and -2 for drug screening applications)

163958-74-5 HCAPLUS RN

L-Alaninamide, N-[(2S)-2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-CNoxopentyl]-3-(2-naphthalenyl)-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L20 ANSWER 6 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

2003:334655 HCAPLUS

DOCUMENT NUMBER:

138:333105

TITLE:

Composition and method for minimizing or avoiding

adverse effects of vesicants

INVENTOR(S):

Lerner, David S.; Schultz, Gregory

PATENT ASSIGNEE(S):

USA

SOURCE:

U.S. Pat. Appl. Publ., 7 pp.

CODEN: USXXCO

DOCUMENT TYPE:

Patent English

LANGUAGE: FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE US 2003083321 A1 20030501 US 2002-256215 20020925 A1 WO 2002-US30597 WO 2003094954 20031120 20020925 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 2001-325015P P 20010925

The invention pertains to compns. and methods to treat the adverse effects of mustard chems. and other toxic compds., such as chemical warfare agents, exposure to which normally induces vesicating type response in mammals. In a rodent eye model at fixed concns. of such a vesicant, compns. comprising (a) a matrix metalloproteinase inhibitor, MMPI, and (b) a protease inhibitor, PI, such as a serine protease inhibitor, SPI, a significant reduction in morbidity is achieved with increased concns. of the compns. of this invention, as compared with an MMPI inhibitor alone or vehicle alone. Furthermore, compns. comprising the MMPI, the SPI, and in addition, an anti-inflammatory compound, in a vehicle appropriate to the type of tissue damage to be protected against from vesicant exposure, achieves both reduction in total tissue damage and inflammation, as compared with anti-inflammatory composition alone. Chems. having more than one property, such as MMPI and anti-inflammatory agent properties, are also disclosed. Certain combinations disclosed are applied to treat injuries due to acids and bases.

IT142880-36-2, Ilomastat

> RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (composition and method for minimizing or avoiding adverse effects of vesicants)

142880-36-2 HCAPLUS RN

Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-CN 2-oxoethyl]-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L20 ANSWER 7 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: DOCUMENT NUMBER:

HCAPLUS 2003:261714

138:292821

TITLE:

Method of preparing basement membrane, method of constructing basement membrane specimen, reconstituted artificial tissue using the basement membrane specimen and process for producing the same

INVENTOR (S):

Mochitate, Katsumi

CODEN: PIXXD2

PATENT ASSIGNEE(S):

Japan Science and Technology Corporation, Japan

SOURCE:

PCT Int. Appl., 85 pp.

DOCUMENT TYPE:

Patent

LANGUAGE:

FAMILY ACC. NUM. COUNT:

Japanese

PATENT INFORMATION:

	PATENT NO.	KIND	DATE	APPLICATION NO. DATE
	WO 2003026712 W: US	A1	20030403	WO 2002-JP9841 20020925
		•	, CY, CZ, , SE, SK,	DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, TR
	JP 2003093050	A2	20030402	JP 2001-292510 20010925
	JP 2003093053	A2	20030402	JP 2001-292676 20010925
	JP 2003169846	A2	20030617	JP 2002-278243 20020924
	JP 2003169847	A2	20030617	JP 2002-278244 20020924
PRIOR	ITY APPLN. INFO	.:		JP 2001-292510 A 20010925
				JP 2001-292675 A 20010925
				JP 2001-292676 A 20010925
				JP 2001-292677 A 20010925
				JP 2002-278243 A 20020924
				JP 2002-278244 A 20020924

A basement membrane is formed by culturing cells on a substrate wherein AΒ the basal face of cells capable of forming a basement membrane has been coated with a polymer having a sugar chain capable of localizing a receptor having an effect of accumulating basement membrane-constituting components. The basement membrane specimen is constructed by treating cells, which are capable of forming a basement membrane and have been adhered to a support via the basement membrane, with a surfactant to solubilize lipid components of the cells and solubilizing proteins remaining on the basement membrane surface with the use of a mixture of an alkali solution with a protease inhibitor. An artificial tissue is obtained by inoculating and culturing desired cells capable of forming a basement membrane. Using a hydrophobic bond adsorption polymer having a linear carbon skeleton with a hydrophobic nature and a functional group capable of reacting with a protein (for example, an alternate copolymer of Me vinyl ether with maleic anhydride), a protein support is tentatively adhered to a plastic surface and a basement membrane specimen or an artificial tissue is formed thereon. Thus, the protein support carrying the basement membrane specimen or the artificial tissue thereon can be phys. separated from the plastic surface when needed. Sugar chain-containing vinyl polymer (PV-GluNAc, PV-CA, or PV-Lam) was applied to fibrous collagen gel formed on a polyethylene terephthalate membrane in a culture well for culture of human pulmonary artery vascular endothelial cells to obtain a basement membrane.

IT 142880-36-2, GM6001

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES

(culture with; method of preparing basement membrane with sugar chain-containing polymer-coated substrate for reconstituted artificial tissue)

RN142880-36-2 HCAPLUS

Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-CN 2-oxoethyl]-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT:

THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS 1 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 8 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

2003:154681 HCAPLUS

DOCUMENT NUMBER:

138:180673

TITLE:

Systems and methods for screening pharmaceutical

chemicals

INVENTOR(S):

Elson, Elliot; McConnaughey, William B.; Wakatsuki,

APPLICATION NO. DATE

Tetsuro

PATENT ASSIGNEE(S):

Washington University in St. Louis, USA

SOURCE:

PCT Int. Appl., 79 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

KIND DATE

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.

	WO	2003	1686	50	A2	2	20030	227		WC	200)2-US	3257 <i>6</i>	51 2	20020	814		
	WO	2003	01686	50	A.	3	20030	612										
		W:	ΑE,	AG,	ΑL,	AM,	ΑT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,	CN,
			CO,	CR,	CŪ,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,
			GM,	HR,	HU,	ID,	ΙL,	IN,	IS,	JΡ,	KE,	KG,	KΡ,	KR,	KZ,	LC,	LK,	LR,
			LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MΖ,	NO,	NΖ,	OM,	PH,
			ΡL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	ТJ,	TM,	TN,	TR,	TT,	TZ,
			UA,	UG,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	ZW,	ΑM,	ΑZ,	BY,	KG,	KZ,	MD,
			RU.	TJ.	TM													
		RW:	GH,	GM,	KE,	LS,	MW,	ΜZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AT,	BE,	BG,
			CH.	CY,	CZ,	DE,	DK,	EE,	ES,	FΙ,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	ΝL,
			PT,	SE,	SK,	TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,
			ΝE,	SN,	TD,	TG												
	US	2003	0643	58	A.	1	2003	0403		US	3 200	02-23	1909'	7	2002	0814		
PRIOF	RIT	Y APP	LN.	INFO	. :				1	JS 20	001-	31232	22P	P	2001	0814		
AB	Αı	metho	d fo	r obt	cain	ing	a re	spons	se o	fat	tiss	ue mo	odel	sys	tem !	to a	n ac	tivator
	in	clude	s co	ntact	ing	a b	oio-a:	rtif	icia	l ti	ssue	mode	el sy	yste	m wi	th a	n ac	tivator
	and	d mea	suri	ng c	ellu	lar	mech	. re	spon	se tl	here	to o	f at	lea	st o	ne o	Ė	
	CO	ntrac	tile	for	ce a	nd t	issu	e st	iffn	ess.	Αı	meth	od fo	or o	btai	ning	a r	esponse
	of	a ti	ssue	mode	el s	yste	m to	an a	acti [,]	vato:	r in	clud	es c	onta	cting	ga		
	hid	o-art	ific	ial '	tiss	ue m	odel	syst	tem '	with	an :	acti	vato:	r an	d me	asur.	ing	
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		stere			-													
	1																	

142880-36-2, GM6001 IT

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(systems and methods for screening pharmaceutical chems.)

142880-36-2 HCAPLUS RN

CN Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L20 ANSWER 9 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

2003:57854 HCAPLUS

DOCUMENT NUMBER:

138:100922

TITLE:

A hydroxamic acid thrombospondin peptide analog that

inhibits aggrecanase activity

INVENTOR(S):

Tortorella, Michael; Wang, Jinhai; Balhorn, Rodney L.

APPLICATION NO. DATE

Enzyme Systems Products, Inc., USA

SOURCE:

PCT Int. Appl., 33 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

KIND DATE

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.

PATENT ASSIGNEE(S):

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WO 2002-US21780 20020709
                              20030123
     WO 2003005956
                        A2
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
              PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
              UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
         TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
              CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
              PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
              NE, SN, TD, TG
                                               US 2002-192283
     US 2003114529
                        A1
                              20030619
                                            US 2001-303989P P 20010709
PRIORITY APPLN. INFO.:
     The present invention concerns the generation of hydroxamic acid
     thrombospondin-peptide analogs that inhibit aggrecanase activity. These
     analogs are useful in the treatment of diseases characterized by cartilage
     degradation, such as osteoarthritis, rheumatoid arthritis
     spondylarthropathies, and septic arthritis. The invention describes a
     novel small mol., enzyme inhibitor that binds both the enzyme and its
     naturally occurring substrate.
     485799-20-0DP, peptide conjugates 485799-20-0P
IT
     485799-21-1P 485799-22-2P 485799-23-3P
     RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
```

(Uses)

CN

(aggrecanase-inhibiting hydroxamic acid thrombospondin peptide analog for treatment of osteoarthritis and spondylarthropathies)

RN 485799-20-0 HCAPLUS

L-Threonine, N-[(2R)-2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-L-valyl-L-glutaminyl-L-alanylglycylglycyl-L-tryptophylglycyl-L-prolyl-L-tryptophylglycyl-L-α-aspartyl-L-seryl-L-seryl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 2-B

RN 485799-20-0 HCAPLUS

L-Threonine, N-[(2R)-2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-L-valyl-L-glutaminyl-L-alanylglycylglycyl-L-tryptophylglycyl-L-prolyl-L-tryptophylglycyl-L-prolyl-L-tryptophylglycyl-L-α-aspartyl-L-seryl-L-seryl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 2-B

RN 485799-21-1 HCAPLUS

L-Threonine, N-[(2R)-2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]L-valyl-L-seryl-L-asparaginyl-L-isoleucyl-L-seryl-L-glutaminyl-Lalanylglycylglycyl-L-tryptophylglycyl-L-prolyl-L-tryptophylglycyl-L-prolylL-tryptophylglycyl-L-α-aspartyl-L-seryl-L-seryl-L-alanyl- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

PAGE 2-B

N H

PAGE 2-A

RN 485799-22-2 HCAPLUS

CN L-Threonine, N-[(2R)-2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-L-valyl-L-leucyl-L-glutaminyl-L-α-aspartyl-L-seryl-L-asparaginyl-L-isoleucyl-L-seryl-L-glutaminyl-L-alanylglycylglycyl-L-tryptophylglycyl-L-prolyl-L-tryptophylglycyl-L-c-aspartyl-L-seryl-L-seryl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

$$\bigcap_{\mathsf{NH}_2}^{\mathsf{O}} \mathsf{NH}_2$$

PAGE 2-C

RN 485799-23-3 HCAPLUS
CN L-Threonine, N-[(2R)-2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]L-valyl-L-methionyl-L-α-aspartyl-L-glutaminyl-L-leucyl-L-glutaminylL-α-aspartyl-L-seryl-L-asparaginyl-L-isoleucyl-L-seryl-L-glutaminylL-alanylglycylglycyl-L-tryptophylglycyl-L-prolyl-L-tryptophylglycyl-Lprolyl-L-tryptophylglycyl-L-α-aspartyl-L-seryl-L-seryl-L-alanyl(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

PAGE 2-C

L20 ANSWER 10 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

2002:850312 HCAPLUS

DOCUMENT NUMBER:

137:346178

TITLE:

Compounds and methods for the modulation of CD154 for

treating thrombosis and inflammation

INVENTOR(S):

Yan, Yibing; Phillips, David; Alaimo, Lisa; Andre,

Patrick; Alves, Veronica

PATENT ASSIGNEE(S):

SOURCE:

U.S. Pat. Appl. Publ., 26 pp.

CODEN: USXXCO

DOCUMENT TYPE:

Patent

USA

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

APPLICATION NO. DATE KIND DATE PATENT NO. _-_-_____ _ _ **_** US 2001-2585 20011130 20021107 US 2002165166 Α1 WO 2002-US13900 20020503 20021114 A2 WO 2002089730 20030213 A3 WO 2002089730 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG EP 2002-734145 20020503 EP 1399466 A2 20040324 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR US 2003-368947 20030217 20040311 Α1 US 2004048803 US 2003-376425 20040415 20030228 US 2004072750 Α1 US 2001-289049P P 20010503 PRIORITY APPLN. INFO.: A 20011130 US 2001-2585 WO 2002-US13900 W 20020503

The present invention relates to compds. that are capable of modulating CD154 mobilization and that are useful for stabilizing the thrombotic process and reducing the activation of cells involved in an inflammatory response. The present invention also relates to methods useful for identifying such compds. The present invention also relates to the treatment of platelets for transfusion with metalloproteinase inhibitors to treat or prevent inflammation. The present invention also includes compns. and methods to treat injury and disease related to such biol. processes. Metalloproteinase inhibitors TAPI-1 and TIMP-2 inhibited platelet aggregation and soluble CD154 release.

US 2003-368947

A2 20030217

IT 142880-36-2, Galardin

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(modulation of CD154 for treating thrombosis and inflammation)

RN 142880-36-2 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

HCAPLUS COPYRIGHT 2004 ACS on STN L20 ANSWER 11 OF 63

ACCESSION NUMBER:

2002:675786 HCAPLUS

DOCUMENT NUMBER:

137:210945

TITLE:

Composition and method using matrix metalloproteinase inhibitors for preventing and treating sinusoidal

obstruction syndrome and radiation-induced liver

disease

INVENTOR(S):

Deleve, Laurie

PATENT ASSIGNEE(S):

University of Southern California, USA

PCT Int. Appl., 14 pp.

SOURCE: CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

P	ATENT			KI	ND	DATE			A	PPLI	CATI	ои ис	0.	DATE				
W	2002			A:	2	2002	0906		W	20	 02-U	S804	1	2002	0227			
W	2002	0678	70	A.	3	20023	1121											
	W:	ΑE,	AG,	AL,	ΑM,	ΑT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,	
		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	
		GM,	HR,	HU,	ID,	IL,	IN,	IS,	JΡ,	KΕ,	KG,	KP,	KR,	KZ,	LC,	LK,	LR,	
		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	OM,	PH,	
		PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	ТJ,	TM,	TN,	TR,	TT,	TZ,	
		UA,	UG,	UZ,	VN,	YU,	ZA,	ZM,	ZW,	AM,	ΑZ,	BY,	KG,	KZ,	MD,	RU,	ТJ,	TM
	RW:	GH,	GM,	KE,	LS,	MW,	ΜZ,	SD,	SL,	SZ,	TZ ,	ŪĠ,	ZM,	ZW,	AT,	ΒE,	CH,	
		CY,	DE,	DK,	ES,	FI,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	TR,	
		BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG	
US	3 2002	1471	58	A:	1	2002	1010		U	S 20	02-8	6072		2002	0227			
E	2 1379	130		A:	2	2004	0114		E	P 20	02-7	1925	7	2002	0227			
	R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,	
		ΙE,	SI,	LT,	LV,	FI,	RO,	MK,	CY,	ΑL,	TR							
PRIORI	ry Apr	LN.	INFO	.:				1	US 2	001-	2717	80P	Ρ	2001	0227			
								1	WO 2	002-	US80	41	W	2002	0227			

Matrix metalloproteinase ("MMP") inhibitors are used to prevent and treat AΒ Sinusoidal Obstruction Syndrome ("SOS"). In particular, the present invention provides a method of preventing and treating chemotherapy- and radiation-induced liver disease. This invention can be given prophylactically to patients who are receiving high dose chemotherapy and/or radiation and who are at risk for SOS or radiation-induced liver disease. This method may also be used to treat patients therapeutically who have developed SOS or radiation-induced liver disease. Because the development of chemotherapy or radiation-induced liver disease limits patient eligibility for several chemotherapeutic drugs, the present

invention increases patient eligibility for many of these drugs. Rats with monocrotaline-induce hepatic venoocclusive disease were treated with doxycycline.

142880-36-2, Ilomastat IT

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(matrix metalloproteinase inhibitors for preventing and treating sinusoidal obstruction syndrome and radiation-induced liver disease)

142880-36-2 HCAPLUS RN

Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-CN2-oxoethyl]-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L20 ANSWER 12 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

2002:556104 HCAPLUS

DOCUMENT NUMBER:

137:109489

TITLE:

Compositions comprising a polypeptide and an active

INVENTOR(S):

Piccariello, Thomas; Olon, Lawrence P.; Kirk, Randal

J.

PATENT ASSIGNEE(S):

USA

SOURCE:

U.S. Pat. Appl. Publ., 34 pp.

CODEN: USXXCO

DOCUMENT TYPE:

Patent English

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE		APPLICATION N	0.	DATE
US 2002099013	A1	20020725		US 2001-93370	8	20010822
PRIORITY APPLN. INFO.	:		US	2000-247556P	P	20001114
			US	2000-247558P	P	20001114
			US	2000-247559P	P	20001114
			US	2000-247560P	P	20001114
			US	2000-247561P	P	20001114
			US	2000-247594P	Р	20001114
			US	2000-247595P	P	20001114
			US	2000-247606P	P	20001114
		•	US	2000-247607P	Ρ	20001114
			US	2000-247608P	P	20001114
,			US	2000-247609P	P	20001114
•			US	2000-247610P	P	20001114
			US	2000-247611P	P	20001114
			US	2000-247612P	P	20001114

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US 2000-247620P
                     20001114
US 2000-247621P
                 Ρ
                     20001114
US 2000-247634P
                 Ρ
                     20001114
US 2000-247635P
                 Ρ
                     20001114
US 2000-247698P
                     20001114
US 2000-247699P
                     20001114
US 2000-247700P
                 Ρ
                     20001114
US 2000-247701P
                 Ρ
                     20001114
US 2000-247702P
                 Р
                     20001114
US 2000-247797P
                 Þ
                     20001114
US 2000-247798P
                 Ρ
                     20001114
US 2000-247799P
                 Ρ
                     20001114
US 2000-247800P
                 P
                     20001114
US 2000-247801P
                 Ρ
                     20001114
US 2000-247802P
                 Ρ
                     20001114
US 2000-247803P
                     20001114
                 P
US 2000-247804P
                     20001114
                 Ρ
US 2000-247805P
                     20001114
                 Ρ
US 2000-247807P
                 Р
                     20001114
US 2000-247832P
                 Р
                     20001114
US 2000-247833P
                     20001114
                 Ρ
US 2000-247926P
                     20001114
                 Р
US 2000-247927P
                     20001114
                 Р
US 2000-247928P
                     20001114
                 P
US 2000-247929P
                 P
                     20001114
US 2000-247930P P
                     20001114
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AB Claimed are compns. comprising a polypeptide and an active agent covalently attached to the polypeptide and a method for delivery of an active agent to a patient by administering the composition to the patient. The peptide is a homopolymer of a naturally occurring amino acid or a heteropolymer of two or more naturally occurring amino acids. In an example, (Glu)n-cephalexin was prepared from Glu(OBut)NCA and cephalexin hydrochloride.

IT 142880-36-2, Ilomastat

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (compns. comprising a polypeptide and an active agent)

RN 142880-36-2 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L20 ANSWER 13 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

2002:521462 HCAPLUS

DOCUMENT NUMBER:

137:88442

TITLE:

Incensole and furanogermacrens and compounds in

treatment for inhibiting neoplastic lesions and

microorganisms

INVENTOR(S):

Shanahan-Pendergast, Elisabeth

PATENT ASSIGNEE(S):

Ire.

SOURCE:

PCT Int. Appl., 68 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PA:	PATENT NO. KIN			ND	DATE			A.	PPI(CATI	ои ис	Ο.	DATE				
									_								
WO	2002	0531	38	A:	2	2002	0711		M	20	02-I	E1		20020	0102		
WO	2002	0531	38	A.	3	2002	0919										
	W:	ΑE,	AG,	ΑT,	AU,	BB,	BG,	CA,	CH,	CN,	CO,	CU,	CZ,	LU,	LV,	MA,	MD,
		UA,	UG,	US,	VN,	YU,	RU,	ТJ,	TM								
	RW:	GH,	GM,	ΚE,	LS,	MW,	SD,	SL,	SZ,	UG,	AT,	BE,	CH,	CY,	DE,	ES,	FI,
		ML,	MR,	ΝE,	SN,	TD,	TG										
EP	1351	678		A:	2	2003	1015		\mathbf{E}	P 20	02-7:	2700'	7	2002	0102		
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	ΝL,	SE,	MC,	PT,
		ΙE,	SI,	LT,	LV,	FΙ,	RO,	MK,	CY,	ΑL,	TR						
PRIORIT	Y APP	LN.	INFO	. :					IE 2	001-	2		Α	2001	0102		
								1	WO 2	002-	IE1		W	2002	0102		

MARPAT 137:88442 OTHER SOURCE(S): .

The invention discloses the use of incensole and/or furanogermacrens, derivs. metabolites and precursors thereof in the treatment of neoplasia, particularly resistant neoplasia and immundysregulatory disorders. These compds. can be administered alone or in combination with conventional chemotherapeutic, antiviral, antiparasite agents, radiation and/or surgery. Incensole and furanogermacren and their mixture showed antitumor activity against various human carcinomas and melanomas and antimicrobial activity against Staphylococcus aureus and Enterococcus faecalis.

142880-36-2, Ilomastat IT

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

142880-36-2 HCAPLUS RN

Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-CN2-oxoethyl]-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

HCAPLUS COPYRIGHT 2004 ACS on STN L20 ANSWER 14 OF 63 ACCESSION NUMBER: 2002:353989 HCAPLUS

DOCUMENT NUMBER:

TITLE:

Cosmetic compositions containing a matrix metalloproteinase inhibitor and estrogen

INVENTOR(S):

Lerner, David S.; Schultz, Gregory

PATENT ASSIGNEE(S):

Quick Med Technologies Inc., USA; University of

Florida Research Foundation, Inc.

SOURCE:

U.S. Pat. Appl. Publ., 5 pp.

CODEN: USXXCO

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002054922	A1	20020509	US 2001-896566	20010629
US 6713074	B2	20040330		

PRIORITY APPLN. INFO.:

US 2000-215087P P 20000629

A cosmetic topical formulation containing a matrix metalloproteinase (MMP) inhibitor, e.g., Ilomastat, is described for diminishing skin wrinkling, fine line, and improving skin tone. The topical formulation also contains a natural estrogen, e.g., a true estrogen compound, such as 17β-estradiol, or an estrogen-like steroid, (such as various phytoestrogens found in herbal prepns.), as opposed to a synthetic estrogen. Other forms of the cosmetic topical formulation of this invention include combinations of synthetic estrogen and MMP inhibitor. Exemplary synthetic estrogens include, but are not limited to, ethinyl estradiol and clomiphene citrate. The cosmetic topical formulation is safe and effective in diminishing wrinkling, and improving skin tone. Certain compns. of this invention are useful for minimizing photodamage to skin, while in other embodiments, the composition according to this invention is useful to prevent or minimize the adverse effects on skin induced by cigarette smoking. For example, a composition comprising black cohosh extract

at.

15 mL of extract per 100 g of gel and 10 mg of Ilomastat and 100 mL of generic cream carrier comprising 35% propylene glycol and the balance water and an acrylate gellant was formed by thorough mixing. The cream was applied to the forearms and then face and neck of a volunteer.

IT 142880-36-2, Ilomastat

> RL: COS (Cosmetic use); BIOL (Biological study); USES (Uses) (cosmetic compns. containing matrix metalloproteinase inhibitor and estrogen for prevention and reduction of skin wrinkles)

142880-36-2 HCAPLUS RN

Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-CN 2-oxoethyl]-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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L20 ANSWER 15 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:
                         2002:332055 HCAPLUS
DOCUMENT NUMBER:
                         136:350543
TITLE:
                         Metalloprotease inhibitors for treatment of
                         angiogenesis
INVENTOR(S):
                         Pan, Duojia; Rubin, Gerald M.; Zhang, Hongbing
                         The Regents of the University of California, USA
PATENT ASSIGNEE(S):
                         PCT Int. Appl., 21 pp.
SOURCE:
                         CODEN: PIXXD2
DOCUMENT TYPE:
                         Patent
                         English
LANGUAGE:
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
     PATENT NO.
                     KIND DATE
                                          APPLICATION NO. DATE
     _____
                                          ______
     WO 2002034289
                     A1 20020502
                                         WO 2001-US45612 20011025
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
             PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
             UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     US 6436629
                      B1 20020820
                                         US 2000-697854 20001027
                                          AU 2002-20098
     AU 2002020098
                       Α5
                            20020506
                                                            20011025
                                         EP 2001-988593
     EP 1333856
                          20030813
                                                            20011025
                     A1
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     US 2002132778
                     A1 20020919
                                          US 2002-68591
                                                            20020206
PRIORITY APPLN. INFO.:
                                        US 2000-697854 A 20001027
                                        WO 2001-US45612 W 20011025
     The invention provides methods and compns. relating to Kuz involvement in
AΒ
     angiogenesis. In various embodiments, the invention provides methods for
     modulating angiogenesis by specifically modulating the activity of Kuz in
     a vertebrate animal predetd. to have a pathogenic angiogenesis; and
     subsequently detecting a resultant angiogenic modulation in the animal.
     Methods are provided for identifying a modulator of angiogenesis by (a)
     contacting an angiogenic assay system comprising a predetd. amount of Kuz
     with a candidate agent, under conditions whereby but for the presence of
     the agent, the system provides a reference angiogenesis; and (b) detecting an
     agent-biased angiogenesis of the system.
TT
     142880-36-2, GM6001 421553-77-7, IC 3
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (metalloprotease inhibitors for treatment of angiogenesis)
     142880-36-2 HCAPLUS
RN
CN
     Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-
```

Absolute stereochemistry.

2-oxoethyl]-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

RN 421553-77-7 HCAPLUS

CN Butanediamide, N1-[(1S)-2-[(2-aminoethyl)amino]-1-methyl-2-oxoethyl]-N4-hydroxy-2-(2-methylpropyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$H_2N$$
 H
 S
 M
 M
 i
 Bu
 O
 O
 M
 H
 OH

REFERENCE COUNT:

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 16 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

2002:332011 HCAPLUS

DOCUMENT NUMBER:

136:355482

TITLE:

Compositions comprising a polypeptide and an active

agent

INVENTOR(S):

Piccariello, Thomas; Olon, Lawrence P.; Kirk, Randall

J.

3

PATENT ASSIGNEE(S):

New River Pharmaceuticals, Inc., USA

SOURCE:

PCT Int. Appl., 98 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

	PAT	ENT	NO.		KI	ND :	DATE			A.	PPLI	CATI	N NC	ο.	DATE			
										_								
1	WO	2002	0342	37	A	1	2002	0502		W	O 20	01-U	S261	42	2001	0822		
		W:	ΑE,	AG,	AL,	AM,	ΑT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,
			CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	ЕĖ,	ES,	FI,	GB,	GD,	GE,	GH,	GM,	HR,
			HU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	ΚP,	KR,	KΖ,	LC,	LK,	LR,	LS,	LT,
			LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	ΜZ,	NO,	NZ,	ΡL,	PT,	RO,	RU,
			SD,	SE,	SG,	SI,	SK,	SL,	ТJ,	TM,	TR,	TT,	TZ,	UA,	UG,	UZ,	VN,	YU,
			ZA,	ZW,	AM,	ΑZ,	BY,	KG,	KZ,	MD,	RU,	ТJ,	TM					
		RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ ,	UG,	ZW,	ΑT,	BE,	CH,	CY,
			DE,	DK,	ES,	FΙ,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	TR,	BF,
			ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GO,	GW,	ML,	MR,	NE,	SN,	TD,	TG	

20000822 20040406 US 2000-642820 US 6716452 **B1** AU 2001086599 20020506 AU 2001-86599 20010822 **A5** EP 2001-966056 20030521 20010822 EP 1311242 Α1

AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.:

US 2000-642820 20000822 Α

WO 2001-US26142 W 20010822

Claimed are compns. comprising a polypeptide and an active agent AB covalently attached to the polypeptide and a method for delivery of an active agent to a patient by administering the composition to the patient. peptide is a homopolymer of a naturally occurring amino acid or a heteropolymer of two or more naturally occurring amino acids. In an example, (Glu)n-cephalexin was prepared from Glu(OBut)NCA and cephalexin hydrochloride.

 $_{
m IT}$ 142880-36-2, Ilomastat

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (compns. comprising a polypeptide and an active agent)

142880-36-2 HCAPLUS RN

Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-CN2-oxoethyl]-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT:

THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS 11 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

HCAPLUS COPYRIGHT 2004 ACS on STN L20 ANSWER 17 OF 63

ACCESSION NUMBER:

2002:184870 HCAPLUS

DOCUMENT NUMBER:

136:221543

TITLE:

Cosmetic compositions containing matrix metalloproteinase inhibitor and estrogens

INVENTOR(S):

Lerner, David S.; Schultz, Gregory

PATENT ASSIGNEE(S):

Quick Med Technologies, Inc., USA; University of

Florida Research Foundation, Inc.

SOURCE:

PCT Int. Appl., 14 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002019982	A2	20020314	WO 2001-US20945	20010629
WO 2002019982	A3	20030724		
1.7 7.77 7.01	7 T 7 M	את אוו אק	עם מת אם מת גם	סס כא כש

AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,

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HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                            A5
                                                       20020322
                                                                                    AU 2001-73115
                                                                                                                       20010629
         AU 2001073115
         EP 1359897
                                            A2
                                                       20031112
                                                                                    EP 2001-952355
                                                                                                                       20010629
                        AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
                         IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
                                                       20040318
                                                                                    JP 2002-524467
                                                                                                                       20010629
PRIORITY APPLN. INFO.:
                                                                               US 2000-215087P P
                                                                                                                       20000629
                                                                               WO 2001-US20945 W
                                                                                                                      20010629
```

The cosmetic topical formulation of this invention is directed toward AB diminishing skin wrinkling, fine lines, improving skin tone, and combinations. Preferably, the topical formulation contains a matrix metalloproteinase inhibitor, MMPI, and advantageously includes a natural estrogen, e.g., a true estrogen compound, such as 17β -estradiol, or an estrogen-like steroid, (such as various phytoestrogens found in herbal prepns.), as opposed to a synthetic estrogen. Other forms of the cosmetic topical formulation of this invention include combinations of synthetic estrogen and MMPI inhibitor. Exemplary synthetic estrogens include, but are not limited to, ethynylestradiol and clomiphene citrate. The cosmetic topical formulation is safe and effective diminishing wrinkling, and improving skin tone. Certain compns. of this invention are useful for minimizing photodamage to skin, while in other embodiments, the composition according to this invention is useful to prevent or minimize the adverse effects on skin induced by cigarette smoking. Thus, a composition contained black cohosh extract (15 mL/100 g gel), 10 mg ilomastat and 100 mL generic cream carrier containing 35% propylene glycol, acrylic gel and the balance water.

IT 142880-36-2, Ilomastat

RL: COS (Cosmetic use); BIOL (Biological study); USES (Uses) (cosmetic compns. containing matrix metalloproteinase inhibitor and estrogens)

RN 142880-36-2 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L20 ANSWER 18 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

2002:72042 HCAPLUS

DOCUMENT NUMBER:

136:135027

TITLE:

Preparation of lysine-based peptide dendrimers as

matrix metalloprotease inhibitors

INVENTOR (S):

Okamachi, Akira; Tamura, Tatsuya; Hayashi, Yoshiki;

Nakamura, Teruo

PATENT ASSIGNEE(S):

Chugai Seiyaku Kabushiki Kaisha, Japan

SOURCE:

PCT Int. Appl., 90 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

Japanese

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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KIND DATE
                                                                                                                         APPLICATION NO. DATE
              PATENT NO.
                                                               A1
                                                                               20020124
                                                                                                                         WO 2001-JP6172
             WO 2002006227
                                                                                                                                                                         20010717
                        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:
                                                                                                                                                             A 20000718
                                                                                                                JP 2000-216790
                                                                                                                                                                 A 20001227
                                                                                                                 JP 2000-398635
OTHER SOURCE(S):
                                                                      MARPAT 136:135027
```

GΙ

$$\begin{array}{c} \text{H} - \text{D-Arg-D-Arg-NH-CH}_2 + \text{CH}_2 - \text{CH}_2 - \text{O} \\ \\ \text{CH}_2 \\ \\ \text{NH} \\ \\ \text{i-Bu} \\ \\ \text{CO} \\ \\ \text{NH-CO} \\ \end{array}$$

Title compds. [HONHCOCHR1CHR2CONHCHR3CONR4CH2(CH2CH2O)3CH2CH2CH2NHCOR; R1 AΒ = H, O, C1-8 alkyl, C1-8 alkoxy, C2-8 alkenyl; R2, R3 independently = cycloalkyl, C1-8 alkyl; R4 = H, C1-4 alkyl; R = alkyleneamino] and salts are prepared and formulation discussed as matrix metalloprotease (MMP) inhibitors useful in improving the retention at an affected part of a living body, such as shoulder periarthritis. Thus, the title compound I was prepared from H2NCH2 [(CH2)20]3CH2CH2CH2NH2, N-9-Fluorenylmethoxycarbonyltryptophan, and $N-\alpha, \omega 1, \omega 2$ -Tris(benzyloxycarbonyl)-D-arqinine and biol. tested for matrix metalloprotease inhibition effect.

387825-45-8P 391902-89-9P 391902-96-8P IT

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of lysine-based peptide dendrimers as matrix metalloprotease inhibitors)

RN 387825-45-8 HCAPLUS

CN D-Argininamide, D-arginyl-N-[(16S)-19-[2-(hydroxyamino)-2-oxoethyl]-16-(1H-indol-3-ylmethyl)-21-methyl-15,18-dioxo-4,7,10-trioxa-14,17-diazadocos-1-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

RN 391902-89-9 HCAPLUS

CN Butanediamide, N1-[(1S,19R)-19,24-diamino-24-imino-1-(1H-indol-3-ylmethyl)-2,18-dioxo-7,10,13-trioxa-3,17,23-triazatetracos-1-yl]-N4-hydroxy-2-(2-methylpropyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

Searched by P. Ruppel

RN 391902-96-8 HCAPLUS

CN D-Argininamide, D-arginyl-D-arginyl-N-[(16S)-19-[2-(hydroxyamino)-2-oxoethyl]-16-(1H-indol-3-ylmethyl)-21-methyl-15,18-dioxo-4,7,10-trioxa-14,17-diazadocos-1-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-B

IT 391902-86-6P 391902-87-7P 391902-88-8P 391902-90-2P 391902-91-3P 391902-92-4P 391902-93-5P 391902-94-6P 391902-95-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

Searched by P. Ruppel

(Reactant or reagent)

(preparation of lysine-based peptide dendrimers as matrix metalloprotease inhibitors)

RN 391902-86-6 HCAPLUS

CN 2,15,18,21-Tetraoxa-3,8,11,25-tetraazahexacosan-26-oic acid, 9-(1H-indol-3-ylmethyl)-6-(2-methylpropyl)-4,7,10-trioxo-1-phenyl-, 1,1-dimethylethyl ester, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

RN 391902-87-7 HCAPLUS

CN Butanediamide, N1-[(1S)-16-amino-1-(1H-indol-3-ylmethyl)-2-oxo-7,10,13-trioxa-3-azahexadec-1-yl]-2-(2-methylpropyl)-N4-(phenylmethoxy)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

-NH₂

RN 391902-88-8 HCAPLUS

CN 2,15,18,21-Tetraoxa-3,8,11,25,31,33-hexaazatetratriacont-31-en-34-oic acid, 9-(1H-indol-3-ylmethyl)-6-(2-methylpropyl)-4,7,10,26-tetraoxo-1-phenyl-27,32-bis[[(phenylmethoxy)carbonyl]amino]-, phenylmethyl ester, (9S,27R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

RN 391902-90-2 HCAPLUS

CN 2,15,18,21-Tetraoxa-3,8,11,25,31,33-hexaazatetratriacont-31-en-34-oic acid, 27-[[(1,1-dimethylethoxy)carbonyl]amino]-9-(1H-indol-3-ylmethyl)-6-(2-methylpropyl)-4,7,10,26-tetraoxo-1-phenyl-32[[(phenylmethoxy)carbonyl]amino]-, phenylmethyl ester, (9S,27R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

$$\begin{array}{c|c} Ph & O & H & Bu-i \\ H & O & HN & O \\ \hline & H & N & O \\ \hline & S & H & CH_2)_3 & O & O & (CH_2)_3 \end{array}$$

PAGE 1-B

RN 391902-91-3 HCAPLUS

CN 2,15,18,21-Tetraoxa-3,8,11,25,31,33-hexaazatetratriacont-31-en-34-oic acid, 27-amino-9-(1H-indol-3-ylmethyl)-6-(2-methylpropyl)-4,7,10,26-tetraoxo-1-phenyl-32-[[(phenylmethoxy)carbonyl]amino]-, phenylmethyl ester, (9S,27R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

RN 391902-92-4 HCAPLUS

CN D-Ornithinamide, N5-[bis[[(phenylmethoxy)carbonyl]amino]methylene]-N2[(phenylmethoxy)carbonyl]-D-ornithyl-N5-[bis[[(phenylmethoxy)carbonyl]amin
o]methylene]-N-[(16S)-16-(1H-indol-3-ylmethyl)-19-(2-methylpropyl)15,18,21-trioxo-24-phenyl-4,7,10,23-tetraoxa-14,17,22-triazatetracos-1-yl](9CI) (CA INDEX NAME)

RN 391902-93-5 HCAPLUS

CN D-Ornithinamide, N5-[bis[[(phenylmethoxy)carbonyl]amino]methylene]-N2[(1,1-dimethylethoxy)carbonyl]-D-ornithyl-N5-[bis[[(phenylmethoxy)carbonyl]amino]methylene]-N-[(16S)-16-(1H-indol-3-ylmethyl)-19-(2-methylpropyl)15,18,21-trioxo-24-phenyl-4,7,10,23-tetraoxa-14,17,22-triazatetracos-1-yl](9CI) (CA INDEX NAME)

$$O$$
 Ph O OBu-t O OBu-t O OPh O Ph O Ph O Ph O Ph O OPh O OP

RN 391902-94-6 HCAPLUS

CN D-Ornithinamide, N5-[bis[[(phenylmethoxy)carbonyl]amino]methylene]-D-ornithyl-N5-[bis[[(phenylmethoxy)carbonyl]amino]methylene]-N-[(16S)-16-(1H-indol-3-ylmethyl)-19-(2-methylpropyl)-15,18,21-trioxo-24-phenyl-4,7,10,23-tetraoxa-14,17,22-triazatetracos-1-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

$$\begin{array}{c|c} Ph & O & H & Bu-i \\ H & O & H & O \\ H & N & O \\ S & & N & (CH_2)_3 & O & O \\ \end{array}$$

RN 391902-95-7 HCAPLUS

CN D-Ornithinamide, N5-[bis[[(phenylmethoxy)carbonyl]amino]methylene]-N2[(phenylmethoxy)carbonyl]-D-ornithyl-N5-[bis[[(phenylmethoxy)carbonyl]amin
o]methylene]-D-ornithyl-N5-[bis[[(phenylmethoxy)carbonyl]amino]methylene]N-[(16S)-16-(1H-indol-3-ylmethyl)-19-(2-methylpropyl)-15,18,21-trioxo-24phenyl-4,7,10,23-tetraoxa-14,17,22-triazatetracos-1-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

$$\begin{array}{c|c} & H & Bu-i \\ & H & O \\ & H & O \\ & & N & O \\ & & & N & O \\ & & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ &$$

REFERENCE COUNT:

109 THERE ARE 109 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L20 ANSWER 19 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

2001:816500 HCAPLUS

DOCUMENT NUMBER:

INVENTOR (S):

135:362539

TITLE:

Functional MRI agents for cancer imaging

Meade, Thomas J.

PATENT ASSIGNEE(S):

Research Corporation Technologies, USA

SOURCE:

PCT Int. Appl., 61 pp.

CODEN: PIXXD2
Patent

DOCUMENT TYPE:

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO. DATE
WO 2001082976	A2	20011108	WO 2001-US14470 20010504
WO 2001082976	A 3	20020510	
W: AU, CA,	JP, US		
RW: AT, BE,	CH, CY	, DE, DK,	ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE,	TR		·
US 6673333	B1	20040106	US 2000-715859 20001117
EP 1278552	A2	20030129	EP 2001-931061 20010504
R: AT, BE,	CH, DE	, DK, ES,	FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI,	LT, LV	, FI, RO,	MK, CY, AL, TR
JP 2003531872	T2	20031028	JP 2001-579849 20010504
PRIORITY APPLN. INFO	. :		US 2000-201816P P 20000504
			US 2000-715859 A1 20001117
			WO 2001-US14470 W 20010504

OTHER SOURCE(S):

MARPAT 135:362539

The invention relates to novel magnetic resonance imaging contrast agents AB for imaging cancer. The agents comprise a Gd(III) ion bound to a first chelator such that the Gd(III) ion has coordination atoms in at least 7 coordination sites and a first tumor-associated activatable guarding moiety (TAAGM) covalently attached to the first chelator which hinders the rapid exchange of water in the remaining coordination sites of the Gd(III) ion. The TAAGM is capable of interacting with a cancer target substance such that the exchange of water in the remaining coordination sites of the first Gd(III) ion is increased. The TAAGM comprises groups which bind to β -glucuronidase.

142880-36-2D, GM 6001, conjugates with gadolinium complexes IΤ RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (functional MRI agents containing enzyme-cleavable groups for use in cancer imaging)

142880-36-2 HCAPLUS RN

Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-CN2-oxoethyl]-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L20 ANSWER 20 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

2001:545522 HCAPLUS

DOCUMENT NUMBER:

135:127214

TITLE:

Inhibitors for plasmodial invasion into erythrocytes Kawai, Satoru; Matsumoto, Jun; Matsuda, Hajime; Terao,

Keiji; Haruki, Kosuke; Yoshino, Kohichiro

PATENT ASSIGNEE(S):

Nippon Organon K. K., Japan

SOURCE:

PCT Int. Appl., 13 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

INVENTOR(S):

Patent Japanese

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
				
WO 2001052891	A1	20010726	WO 2001-JP336	20010119
t.t TD				-

W: JP PRIORITY APPLN. INFO.:

A 20000120 JP 2000-48304

Inhibitors against the invasion of plasmodium into erythrocytes, contain as the active ingredient compds. having an inhibitory effect on metal-containing enzymes (in particular, zinc-containing enzymes). inhibitors inhibit the process of the invasion into erythrocytes and proliferation therein of plasmodium after the infection, and the process of the invasion into erythrocytes and proliferation therein of the merozoites thus formed, thereby achieving preventive and therapeutic

effects on the onset of malaria. Claimed compds. include [4-(N-hydroxyamino)-2(R)-isobutyl-3(S)-methylsuccinyl]-L-phenylglycine-Nmethylamide and N-[2,2-dimethyl-1(S)-(N-methylcarbamoyl)propyl]-N,3(S)dihydroxy-2(R)-isobutylsuccinamide.

IT 351316-90-0

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

(hydroxamic acids as inhibitors for plasmodial invasion into ervthrocytes)

RN

351316-90-0 HCAPLUS Glycinamide, N-[(2R)-2-[(1S)-2-(hydroxyamino)-1-methyl-2-oxoethyl]-4-CN methyl-1-oxopentyl]-L-phenylalanyl-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT:

THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS 13 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

HCAPLUS COPYRIGHT 2004 ACS on STN L20 ANSWER 21 OF 63

ACCESSION NUMBER:

2001:142139 HCAPLUS

DOCUMENT NUMBER:

134:188234

TITLE:

Metalloproteinase inhibitors containing hydroxamic

INVENTOR(S):

Fujisawa, Tetsunori; Kotake, Shinjiro; Hongo, Kazuya;

Ito, Hajime; Otani, Miwa; Yasuda, Junko; Morikawa,

Tadanori

PATENT ASSIGNEE(S):

Fuji Pharmaceutical Industries Co., Ltd., Japan

SOURCE:

Jpn. Kokai Tokkyo Koho, 68 pp.

CODEN: JKXXAF

DOCUMENT TYPE:

Patent

LANGUAGE ·

Japanese

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

APPLICATION NO. DATE PATENT NO. KIND DATE _____ JP 2000-173115 20000609 JP 2001055327 A2 20010227 PRIORITY APPLN. INFO .: JP 1999-165675 A 19990611 MARPAT 134:188234 OTHER SOURCE(S):

The inhibitors, useful for treatment of ulcerative colitis, autoimmune diseases, osteoarthritis, malignant tumor, psoriasis, and diabetes mellitus, contain R1ONR2COCHR3CHR4CONHCH(CR6R7R8)COR5 [I; R1 = H, protective group; R2 = H, protective group; R3, R7, R8 = H, OH, (un) substituted alkyl, (un) substituted aralkyl; R4 = (un) substituted alkyl, (un) substituted aralkyl; R5 = OR9, NR10R11; R9 = H, (un) substituted alkyl, (un) substituted aralkyl, etc.; R10, R11 = H, (un) substituted (cyclo)alkyl, heterocyclyl, etc.; R6 = H, OH, amino, etc.], their salts, or solvates. I show good bioavailability. I monoacetate [R1 = R2 = R7 =

R8 = H, R3 = Me, R4 = iso-Bu, R5 = NHMe, R6 = (CH2)2NHC(:NH)NH2] (preparation given) in vitro inhibited collagenase (MMP-1) with IC50 of 5 nM. Formulation examples are given.

TT 228260-68-2P 228261-56-1P 328066-14-4P 328066-18-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of hydroxamic acids as metalloproteinase inhibitors)

RN 228260-68-2 HCAPLUS

CN Butanediamide, N1-[(1S)-1-[[[2-(dimethylamino)ethyl]amino]carbonyl]-5-[(1-iminoethyl)amino]pentyl]-N4-hydroxy-2-(2-methylpropyl)-3-(3-phenylpropyl)-, (2R)-, diacetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 228260-67-1 CMF C29 H50 N6 O4

Absolute stereochemistry.

CM 2

CRN 64-19-7 CMF C2 H4 O2

RN 228261-56-1 HCAPLUS

CN Butanediamide, 2-[3-(4-aminophenyl)propyl]-N4-[(1S)-1-[[[2-(dimethylamino)ethyl]amino]carbonyl]-5-[(1-iminoethyl)amino]pentyl]-N1-hydroxy-3-(2-methylpropyl)-, (3R)-, triacetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 228261-55-0 CMF C29 H51 N7 O4

CM 2

CRN 64-19-7 CMF C2 H4 O2

RN 328066-14-4 HCAPLUS

CN Butanediamide, N1-[(1S)-1-[[4-(aminomethyl)phenyl]methyl]-2-[[2-(dimethylamino)ethyl]amino]-2-oxoethyl]-N4-hydroxy-2,3-bis(2-methylpropyl)-, (2R)-, diacetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 228261-50-5 CMF C26 H45 N5 O4

Absolute stereochemistry.

CM 2

CRN 64-19-7 CMF C2 H4 O2

RN 328066-18-8 HCAPLUS

CN Butanediamide, N1-[(1S)-2-[[2-(dimethylamino)ethyl]amino]-1-[[4-[[(1-iminoethyl)amino]methyl]phenyl]methyl]-2-oxoethyl]-N4-hydroxy-2,3-bis(2-methylpropyl)-, (2R)-, diacetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 328066-17-7 CMF C28 H48 N6 O4

Absolute stereochemistry.

CM 2

CRN 64-19-7 CMF C2 H4 O2

HO-C-CH3

L20 ANSWER 22 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

2001:78256 HCAPLUS

DOCUMENT NUMBER:

134:136715

TITLE:

Solutions and methods for inhibition of pain,

inflammation and cartilage degradation

INVENTOR(S):

Demopulos, Gregory A.; Palmer, Pamela P.; Herz,

Jeffrey M.

PATENT ASSIGNEE(S):

Omeros Medical Systems, Inc., USA

SOURCE:

PCT Int. Appl., 105 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

': 14

PATENT INFORMATION:

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KIND
        PATENT NO.
                                               DATE
                                                                        APPLICATION NO. DATE
                                     ____
                                               _____
                                                                         -----
        WO 2001007067
                                      A2
                                               20010201
                                                                        WO 2000-US19864 20000721
        WO 2001007067
                                      Α3
                                               20010329
              W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                                                      EP 2000-947581 20000721
        EP 1200127
                                     A2 20020502
                     AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL
        JP 2003505427
                                      T2
                                               20030212
                                                                         JP 2001-511950
                                                                                                      20000721
        US 2003235589
                                      A1
                                               20031225
                                                                         US 2003-356649
                                                                                                      20030131
PRIORITY APPLN. INFO.:
                                                                    US 1999-144904P P
                                                                                                      19990721
                                                                    US 1998-105026P P
                                                                                                     19981020
                                                                    US 1998-107256P P 19981105
                                                                    WO 1999-US24625 A2 19991020
                                                                    WO 1999-US26330 A2 19991105
                                                                    WO 2000-US19864 W 20000721
                                                                                                 A2 20010420
                                                                    US 2001-839633
                                                                    US 2002-31546
                                                                                                 A2 20020118
                                                                    US 2002-353552P P 20020201
```

AB Methods and solns. for inhibiting a variety of pain and inflammation processes at wounds from general surgical procedures including arthroscopic procedures, and for inhibiting cartilage degradation are disclosed. The solns. preferably include multiple pain and inflammation inhibitory at dilute concentration in a physiol. carrier, such as saline or lactated Ringer's solution The solution may be applied by continuous irrigation

of a wound during a surgical procedure for preemptive inhibition of pain and while avoiding undesirable side effects associated with oral, i.m., s.c. or i.v. application of larger doses of the agents. Alternatively, for combinations of cartilage degradation inhibitors, the solns. may be injected directly into the joint. An irrigation solution for arthroscopy was prepared containing SB203580 (MAP kinase inhibitor) 200, U-24522 (matrix metalloproteinase inhibitor) 200, and TGF- β 2 200 nM.

IT 106314-87-8, U-24522

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (solns. and methods for inhibition of pain, inflammation and cartilage degradation)

RN 106314-87-8 HCAPLUS

CN L-Phenylalaninamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-L-leucyl- (9CI) (CA INDEX NAME)

L20 ANSWER 23 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

2000:861771 HCAPLUS

DOCUMENT NUMBER:

134:14908

TITLE:

In vitro cell culture device including cartilage and

methods of using the same

INVENTOR(S):

Hicks, Wesley L., Jr.

PATENT ASSIGNEE(S):

Research Foundation of State University of New York,

SOURCE:

PCT Int. Appl., 39 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAT	CENT :	NO.		KII	ND	DATE			A.	PPLI	CATI	ON NC	ο.	DATE			
									7.7					2000	1E2C		
WO	2000																
	W:													CH,			
														HR,			
														LT,			
														SD,			
		SK,	SL,	ТJ,	TM,	TR,	TT,	ΤŹ,	UA,	UG,	UZ,	VN,	YU,	ZA,	ZW,	AM,	AZ,
		BY,	KG,	KΖ,	MD,	RU,	TJ,	ΜT									
•	RW:													ΑT,			
														PT,	SE,	BF,	ВJ,
						GΑ,											
	6312																
US	2002	0098	06	A	1	2002	0124		U	S 20	01-9	5399	0	2001	0918		
US	6465	205		B	2	2002	1015										
ORITY	APP	LN.	INFO	. :				•	US 1	999-	1366	10P	P	1999	0527		

PRIORITY APPLN US 2000-579805 A3 20000526

The present invention relates to an in vitro cell culture device which includes a vessel comprising an inner surface, a layer of cartilage disposed on at least a portion of said inner surface, the layer of cartilage including a plurality of chondrocytes in an extracellular matrix, and a growth medium in the vessel, the layer of cartilage being bathed in the growth medium. Also disclosed is a composite cell culture prepared from the in vitro cell culture device, the composite cell culture includes a first layer including chondrocytes in an extracellular matrix, a second layer disposed on the first layer and including type I collagen, and a third layer disposed on the second layer and including cells at least partially covering the second layer. Further aspects of the present invention relate to methods of preparing an in vitro composite cell culture, methods of screening putative therapeutic agents for activity in promoting re-epithelialization of cartilaginous tissues, and methods of screening putative therapeutic agents for activity in inhibiting growth factors or

proteinases.

IT 142880-36-2, GM6001

RL: BSU (Biological study, unclassified); BUU (Biological use,

unclassified); BIOL (Biological study); USES (Uses)

(In vitro cell culture device including cartilage and methods of using same)

RN 142880-36-2 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT:

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 24 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

2000:592569 HCAPLUS

DOCUMENT NUMBER:

133:183019

TITLE:

Connective tissue softening with matrix

metalloproteinase inhibitors Ferguson, Mark William James

PATENT ASSIGNEE(S):

Victoria University of Manchester, UK

SOURCE:

PCT Int. Appl., 17 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

INVENTOR(S):

LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND DATE		
WO 2000048617	A2 20000824	WO 2000-GB474 20000	0214
WO 2000048617	A3 20010208		
W: AE, AL,	AM, AT, AU, AZ,	BA, BB, BG, BR, BY, CA, CH,	CN, CR, CU,
CZ, DE,	DK, DM, EE, ES,	FI, GB, GD, GE, GH, GM, HR,	HU, ID, IL,
IN, IS,	JP, KE, KG, KP,	KR, KZ, LC, LK, LR, LS, LT,	LU, LV, MA,
MD, MG,	MK, MN, MW, MX,	NO, NZ, PL, PT, RO, RU, SD,	SE, SG, SI,
SK, SL,	TJ, TM, TR, TT,	TZ, UA, UG, US, UZ, VN, YU,	ZA, ZW, AM,
AZ, BY,	KG, KZ, MD, RU,	TJ, TM	
RW: GH, GM,	KE, LS, MW, SD,	SL, SZ, TZ, UG, ZW, AT, BE,	CH, CY, DE,
DK, ES,	FI, FR, GB, GR,	IE, IT, LU, MC, NL, PT, SE,	BF, BJ, CF,
CG, CI,	CM, GA, GN, GW,	ML, MR, NE, SN, TD, TG	
EP 1152757	A2 20011114	EP 2000-903808 20000	0214
R: AT, BE,	CH, DE, DK, ES,	FR, GB, GR, IT, LI, LU, NL,	SE, MC, PT,
IE, SI,	LT, LV, FI, RO		
JP 2002537268	T2 20021105	JP 2000-599407 20000	0214
US 6455569	B1 20020924	US 2001-913713 20010	0817

PRIORITY APPLN. INFO.:

GB 1999-3598 A 19990218 W 20000214 WO 2000-GB474

Matrix Metalloproteinase Inhibitors are used in the prevention or AB treatment of connective tissue softening and also for the maintenance of sutures in such connective tissues. The connective tissue may be a tendon, ligament or cartilage. Example inhibitors are batimastat or galardin.

142880-36-2, Galardin IT

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (connective tissue softening with matrix metalloproteinase inhibitors)

RN142880-36-2 HCAPLUS

Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-CN2-oxoethyl]-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L20 ANSWER 25 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

2000:68329 HCAPLUS

DOCUMENT NUMBER:

132:117536

TITLE:

Hydroxamic acid derivatives as novel remedies for

allergic diseases

INVENTOR(S):

Igeta, Katsuhiro; Tobetto, Kenji; Saiki, Ikuo; Odake,

Shinjiro; Fujisawa, Tetsunori; Matsuo, Tetsu; Oku,

PATENT ASSIGNEE(S):

Fuji Yakuhin Kogyo Kabushiki Kaisha, Japan; Maruho

Co., Ltd.

SOURCE:

PCT Int. Appl., 193 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

Japanese

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO	ο.	ΚI	ND :	DATE APPLICATION NO. DATE													
		-										·································					
WO 200000	03703	A	1	2000	0127		W	O 19:	99-J	P385	1	1999	0716				
W: A	AE, AL	, AM,	ΑT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CU,	CZ,		
	DE, DK																
j	JP, KE	, KG,	KP,	KR,	ΚZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	MD,	MG,	MK,		
	MM, MW																
7	rm, TR	, TT,	UA,	UG,	US,	UΖ,	VN,	YU,	ZA,	ZW,	AM,	ΑZ,	BY,	KG,	KZ,		
N	MD, RU	, TJ,	TM														
RW: C	GH, GM	, KE,	LS,	MW,	SD,	SL,	SZ,	ŪĠ,	ZW,	ΑT,	BE,	CH,	CY,	DE,	DK,		
H	ES, FI	, FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,	CF,	CG,		
	CI, CM	, GA,	GN,	GW,	ML,	MR,	NΕ,	SN,	TD,	TG							
CA 233785	59	Α	A	2000	0127		C	A 19	99-2	3378	59	1999	0716				

AU 9946531 A1 20000207 AU 1999-46531 19990716 EP 1101492 A1 20010523 EP 1999-929875 19990716

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.:

JP 1998-218662 A 19980717 WO 1999-JP3851 W 19990716

Drugs characterized by containing hydroxamic acid derivs. as the active ingredient which are efficacious in treating and/or preventing allergies, in particular, type I and/or type II allergies, etc. These drugs exert therapeutic and/or preventive effects on inflammation, rhinitis, conjunctivitis, bronchial asthma, atopic dermatitis (dermatitis, enteritis, etc.) and allergic digestive inflammation. Use of these drugs achieves the effects of: (A) inhibiting the proliferation of colonies of blood cells (lymphocytes, etc.) in an affected part; and/or (B) relieving inflammation caused by the migration, infiltration, accumulation, etc. of blood cells (lymphocytes, etc.) into an affected part; and/or (C) regulating the pathophysiol. functions of cells such as blood cells (lymphocytes, etc.), Langerhans cells and dendritic cells; and/or (D) regulating the production of antibodies, in particular, IgE in the plasma, thus being useful in treating and/or preventing diseases or pathol. conditions in the affected parts.

IT 228260-68-2P 228261-52-7P 228261-56-1P 256412-42-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(hydroxamic acid derivs. as novel remedies for allergic diseases)

RN 228260-68-2 HCAPLUS

CN Butanediamide, N1-[(1S)-1-[[[2-(dimethylamino)ethyl]amino]carbonyl]-5-[(1-iminoethyl)amino]pentyl]-N4-hydroxy-2-(2-methylpropyl)-3-(3-phenylpropyl)-, (2R)-, diacetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 228260-67-1 CMF C29 H50 N6 O4

Absolute stereochemistry.

CM 2

CRN 64-19-7 CMF C2 H4 O2

RN 228261-52-7 HCAPLUS

CN Butanediamide, N-[(1S)-2-[[2-(dimethylamino)ethyl]amino]-1-[[4-[[(1-iminoethyl)imino]methyl]phenyl]methyl]-2-oxoethyl]-N'-hydroxy-2,3-bis(2-methylpropyl)-, (2R)-, diacetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 228261-51-6 CMF C28 H46 N6 O4

Absolute stereochemistry.

Double bond geometry unknown.

CM 2

CRN 64-19-7 CMF C2 H4 O2

RN 228261-56-1 HCAPLUS

CN Butanediamide, 2-[3-(4-aminophenyl)propyl]-N4-[(1S)-1-[[[2-(dimethylamino)ethyl]amino]carbonyl]-5-[(1-iminoethyl)amino]pentyl]-N1-hydroxy-3-(2-methylpropyl)-, (3R)-, triacetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 228261-55-0 CMF C29 H51 N7 O4

CM 2

CRN 64-19-7 CMF C2 H4 O2

RN 256412-42-7 HCAPLUS

CN Butanediamide, N-[(1S)-1-[[4-(aminomethyl)phenyl]methyl]-2-[[2-(dimethylamino)ethyl]amino]-2-oxoethyl]-N'-hydroxy-2,3-bis(2-methylpropyl)-, (2R,3S)-, monoacetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 256412-41-6 CMF C26 H45 N5 O4

Absolute stereochemistry.

CM 2

CRN 64-19-7 CMF C2 H4 O2

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O
||
HO-- C-- CH<sub>3</sub>
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REFERENCE COUNT:

6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 26 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

2000:15004 HCAPLUS

DOCUMENT NUMBER:

132:73666

TITLE:

Ophthalmic uses of PPAR- γ agonists and

antagonists

INVENTOR(S):

Pershadsingh, Harrihar A.; Levy, Daniel E.

PATENT ASSIGNEE(S):

Photogenesis, Inc., USA PCT Int. Appl., 43 pp.

SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.				KIND DATE			APPLICATION NO.						DATE					
									-									
WO	2000	0001	94	A	1.	2000	0106		W) 19	99-U	5142	52	19990625				
	W:	AL,	AM,	AT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CU,	CZ,	DE,	
		DK,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	
		ΚE,	KG,	ΚP,	KR,	ΚZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	MD,	MG,	MK,	MN,	
		MW,	MX,	NO,	ΝZ,	PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	TJ,	TM,	
		TR,	TT,	UA,	ŪĠ,	US,	UΖ,	VN,	YU,	ZW,	AM,	ΑZ,	ΒY,	KG,	ΚZ,	MD,	RU,	
		ТJ,	TM															
	RW:	GH,	GM,	KE,	LS,	MW,	SD,	SL,	SZ,	UG,	ZW,	AT,	BE,	CH,	CY,	DE,	DK,	
		ES,	FI,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	ΝL,	PT,	SE,	BF,	ВJ,	CF,	CG,	
		CI,	CM,	GA,	GN,	GW,	ML,	MR,	ΝE,	SN,	TD,	TG						
AU	9947	134		Α	1	2000	0117		Al	U 19	99-4	7134		1999	0625			
US	6316	465		В	1	2001	1113		U	S 19	99-3	1238	1	1999	0628			
PRIORIT	Y APP	LN.	INFO	. :				1	US 1:	998-	9093	7P	P	1998	0627			
								1	US 1	998-	9093	7	P	1998	0627			
								1	WO 1:	999-	US14:	262	W	1999	0625			

OTHER SOURCE(S): MARPAT 132:73666

Methods are disclosed for treating diseases of ocular tissues expressing the nuclear receptor PPAR- γ , by inhibiting the inflammatory response, the neovascularization and angiogenesis, and programmed cell death (apoptosis) in these target tissues, comprising administering to a human or animal in need of treatment an effective amount of a compound that modifies the activity of PPAR- γ , or a pharmaceutically acceptable salt or solvate thereof. Novel compds. and methods for their synthesis are provided.

IT 253587-93-8

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(ophthalmic uses of PPAR- γ agonists and antagonists)

RN 253587-93-8 HCAPLUS

CN Butanediamide, N4-[(1S)-1-[[[2-[[(3,4-dihydro-6-hydroxy-2,5,7,8-tetramethyl-2H-1-benzopyran-2-yl)carbonyl][2-[4-[[(5R)-2,4-dioxo-5-thiazolidinyl]methyl]phenoxy]ethyl]amino]ethyl]amino]carbonyl]-2,2-dimethylpropyl]-N1,2-dihydroxy-3-(2-methylpropyl)-, (2S,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT:

THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

HCAPLUS COPYRIGHT 2004 ACS on STN L20 ANSWER 27 OF 63

1

ACCESSION NUMBER:

1999:583142 HCAPLUS

DOCUMENT NUMBER:

131:223493

TITLE:

Peptide derivatives for prevention or treatment of

connective tissue disease

INVENTOR(S):

Matsuo, Konomi; Yamamoto, Minoru; Ikeda, Shoji

PATENT ASSIGNEE(S):

Kanebo, Ltd., Japan

SOURCE:

Jpn. Kokai Tokkyo Koho, 16 pp.

CODEN: JKXXAF

DOCUMENT TYPE:

LANGUAGE:

Patent Japanese

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

OTHER SOURCE(S):

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 11246436	A2	19990914	JP 1998-71445	19980304
PRIORITY APPLN. INFO.	: .		JP 1998-71445	19980304

MARPAT 131:223493

Peptide derivs. such as [4-(N-hydroxyamino)-2-[R]-isobutylsuccinyl]-Lphenylalanyl-L-alaninal [prepns. given] as matrix metalloprotease and cathepsin for prevention or treatment of connective tissue disease are claimed. The compds. lowered the urinary hydroxyproline excretion in mice with osteoporosis. Capsules were formulated containing [4-(N-hydroxyamino)-2-

[R]-isobutylsuccinyl]-L-phenylalanyl-L-alaninal 100, lactose 35, corn starch 60 and magnesium stearate 5 weight parts.

244021-29-2P 244021-30-5P 244021-31-6P IT

244021-32-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(peptide derivs. for prevention or treatment of connective tissue disease)

RN ·244021-29-2 HCAPLUS

L-Alaninamide, N-[(2R)-4-methyl-1-oxo-2-[2-oxo-2-CN

[(phenylmethoxy)amino]ethyl]pentyl]-L-phenylalanyl-N-methoxy-N-methyl-

(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 244021-30-5 HCAPLUS

CN L-Alaninamide, N-[(2R)-4-methyl-1-oxo-2-[2-oxo-2-[(phenylmethoxy)amino]ethyl]pentyl]-L-leucyl-N-methoxy-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 244021-31-6 HCAPLUS

CN L-Leucinamide, N-[(2R)-4-methyl-1-oxo-2-[2-oxo-2-[(phenylmethoxy)amino]ethyl]pentyl]-L-phenylalanyl-N-methoxy-N-methyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$\begin{array}{c|c} OMe \\ \hline \\ i-Bu \\ S \\ \hline \\ H \\ \hline \\ Ph \\ i-Bu \\ R \\ \hline \\ O \\ O \\ Ph \\ H \\ \end{array}$$

RN 244021-32-7 HCAPLUS

CN Glycinamide, N-[(2R)-4-methyl-1-oxo-2-[2-oxo-2-[(phenylmethoxy)amino]ethyl]pentyl]-L-phenylalanyl-N-methoxy-N-methyl-(9CI) (CA INDEX NAME)

L20 ANSWER 28 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1999:511239 HCAPLUS

DOCUMENT NUMBER:

131:155326

TITLE:

Crystalline TNF- α -converting enzyme and uses

thereof

INVENTOR(S):

Black, Roy A.; Paxton, Raymond James; Bode, Wolfram; Maskos, Klaus; Fernandez-Catalan, Carlos; Chen, James

Ming; Levin, Jeremy Ian

PATENT ASSIGNEE(S):

Immunex Corporation, USA; Max-Planck-Institute for Biochemistry; American Home Products Corporation

PCT Int. Appl., 99 pp.

SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PA	TENT	NO.		KI	ND	DATE		APPLICATION NO.					DATE				
	9940									0 19	 99-บ	S218	5	1999	0203		
WO	9940																
	W:	ΑL,	AM,	AT,	AU,	ΑZ,	ВA,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CU,	CZ,	DE,
														KE,			
		ΚZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	MD,	MG,	MK,	MN,	MW,	MX,	NO,	NΖ,
		ΡL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	TJ,	TM,	TR,	TT,	UA,	UG,
			UΖ,														
	RW:	GH,	GM,	KE,	LS,	MW,	SD,	SZ,	UG,	ZW,	ΑT,	BE,	CH,	CY,	DE,	DK,	ES,
												SE,	BF,	BJ,	CF,	CG,	CI,
		CM,	GA,	GN,	GW,	ML,	MR,	NE,	SN,	TD;	TG						
CA	2319	040		A	A	1999	0812		C	A 19	99-2	3190	40	1999	0203		
AU	9925	740		Α	1	1999	0823		A	U 19	99-2	5740		1999			
ZA	9900	851		Α		1999	0825		Z	A 19	99-8	51		1999	0203		
EP	1053	304		Α	2	2000	1122		E	P 19	99-9	0561	5	1999	0203		
	R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,
		ΙE,	FI														
	5059			Α		2003								1999			
	2004													1999			
	2002					2002								1999			
	2000													2000			•
US	2003	0046	51	Α	1	2003	0102			S 20				2001			
IORIT	Y APF	LN.	INFO	.:						998-		-		1998			
														1998			
										.999-			_	1999			
										.998-			_	1998			
										999-			• •	1999			
		•												1999			
														2000			
. Δ	tumor	nec	rosi	s fa	ctoi	c-α. c	onve	rtin	a en	ızvme	TA)	CE)	is t	orodu	ced,		

AB A tumor necrosis factor- α converting enzyme (TACE) is produced,

purified, and crystallized The three-dimensional coordinates of the crystal are obtained by x-ray diffraction. The coordinates can be recorded on a computer readable medium, or are part of a video memory, where they can be used as part of a system for studying TACE. The coordinates are also used in designing, screening, and developing compds. that associate with TACE.

187034-31-7 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(crystal structure of TNF- α -converting enzyme and its uses)

187034-31-7 HCAPLUS RN

L-Alaninamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-3-CN methyl-L-valyl-N-(2-aminoethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L20 ANSWER 29 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1999:421569 HCAPLUS

DOCUMENT NUMBER:

131:68144

TITLE:

IT

Angiotensin-converting enzyme inhibitor-matrix

metalloproteinase inhibitor combinations for treatment of fibrosis, ventricular dilation, and heart failure Peterson, Joseph Thomas, Jr.; Pressler, Milton Lethan

INVENTOR(S):

Warner-Lambert Company, USA

PATENT ASSIGNEE(S):

SOURCE:

PCT Int. Appl., 156 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

LANGUAGE:

Patent

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND DATE	APPLICATION NO. DATE
WO 9932150	WO 1998-US23993 19981110	
		CA, CN, CU, CZ, EE, GE, HR, HU, ID, IL,
IS, JP,	KP, KR, LC, LK,	LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL,
RO, SG,	SI, SK, SL, TR,	TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG,
,	RU, TJ, TM	
		SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
		LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
	GN, GW, ML, MR,	
CA 2305436	AA 19990701	CA 1998-2305436 19981110
AU 9915220	A1 19990712	AU 1999-15220 19981110
AU 751701	B2 20020822	•
BR 9814422	A 20001010	BR 1998-14422 19981110
EP 1047450	A1 20001102	EP 1998-959416 19981110
EP 1047450	B1 20021002	

AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI JP 2000-525140 19981110 JP 2001526245 T2 20011218 NZ 1998-503962 NZ 503962 Α 20020328 19981110 AT 1998-959416 AT 225187 \mathbf{E} 20021015 19981110 ES 1998-959416 ES 2184340 Т3 20030401 19981110 ZA 9811794 Α 19990629 ZA 1998-11794 19981222 US 2000-485253 US 6133304 Α 20001017 20000207 MX 2000-3736 MX 200003736 Α 20001020 20000417

NO 2000003256
PRIORITY APPLN. INFO.:

US 1997-68594P P 19971223 WO 1998-US23993 W 19981110

20000622

NO 2000-3256

OTHER SOURCE(S):

MARPAT 131:68144

20000622

AB Combinations of ACE inhibitors and MMP inhibitors are useful to slow and reverse the process of fibrosis, ventricular dilation, and heart failure in mammals.

IT 106314-87-8, U24522 142880-36-2, Galardin

Α

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(ACE inhibitor-matrix metalloproteinase inhibitor combinations for treatment of fibrosis, ventricular dilation, and heart failure)

RN 106314-87-8 HCAPLUS

CN L-Phenylalaninamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$H_2N$$
 S
 H
 i
 $-Bu$
 O
 i
 H
 O
 M
 H
 O
 M
 H

RN 142880-36-2 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

6

REFERENCE COUNT:

THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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HCAPLUS COPYRIGHT 2004 ACS on STN
L20 ANSWER 30 OF 63
                        1999:404921 HCAPLUS
ACCESSION NUMBER:
```

DOCUMENT NUMBER:

131:73975

TITLE:

Preparation of N-[4-(hydroxyamino) succinyl] amino acid amide derivatives as metalloproteinase inhibitors

INVENTOR(S):

Fujisawa, Tetsunori; Odake, Shinjiro; Hongo, Kazuya;

Ohtani, Miwa; Yasuda, Junko; Morikawa, Tadanori

PATENT ASSIGNEE(S):

Fuji Yakuhin Kogyo Kabushiki Kaisha, Japan

SOURCE:

PCT Int. Appl., 172 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

Japanese

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

	PAC	CENT	NO.		KIN	1D	D DATE APPLICATION NO.							DATE					
	WO						1999												
		W:					ΑZ,												
			DK,	EE,	ES,	FI,	GB,	GD,	GΕ,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	
							LC,												
			MX,	NO,	NZ,	PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	ΤJ,	TM,	TR,	
			TT,	UA,	UG,	US,	UZ,	VN,	YU,	ZW,	AM,	ΑZ,	BY,	KG,	KZ,	MD,	RU,	ТJ,	TM
•		RW:	GH,	GM,	KΕ,	LS,	MW,	SD,	SZ,	UG,	ZW,	ΑT,	BE,	CH,	CY,	DE,	DK,	ES,	
			FI,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,	CF,	CG,	CI,	
							ML,								•				
							1999								1998	1211			
	AU	9915	066		A.	1	1999	0705		Α	U 19	99-1	5066		1998	1211			
	AU	7530	17		B	2	2002	1003											
							2000			J	P 19	98-3	7494	5	1998	1211			
	EΡ	1038	864		A.	1	2000	0927		E	P 19	98-9	5918	1	1998	1211			
		R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,	
			ΙĒ,	FI															
	BR	9813	554		Α		2001	0724		В	R 19	98-1	3554		1998	1211			
	RU	2200	154		C	2	2003	0310		R	U 20	00-1	1832	0	1998	1211			
PRIO										JP 1	997-	3623	64	Α	1997	1212			
										JP 1	998-	2186	76	Α	1998	0717			
										WO 1	998-	JP56	20	W	1998	1211			

MARPAT 131:73975 OTHER SOURCE(S):

> Claimed are compds. represented by general formula R1ONR2COCHR3CHR4CONHCH(CR7R8R9)CONR5R6 or salts thereof [I; wherein R1 represents hydrogen, (un) substituted aralkyl, tri-substituted silyl, tetrahydropyranyl, (un) substituted aralkyloxycarbonyl, (un) substituted alkyl, or a hydroxy-protective group; R2 represents hydrogen, (un) substituted aralkyloxycarbonyl, (un) substituted alkyloxycarbonyl, 9-fluorenylmethyloxycarbonyl, or an amino-protective group; R3, R7 and R8 represent each hydrogen, hydroxy, (un) substituted alkyl, or (un) substituted aralkyl; R4 represents (un) substituted alkyl or (un) substituted arylalkyl; R5 and R6 are the same or different and each represents hydrogen, (un) substituted alkyl, (un) substituted cycloalkyl, (un) substituted heterocyclyl, or an amino-protective group; or NR5R6 represents an (un) substituted heterocyclyl; and R9 represents hydrogen, hydroxy, amino, or -X-Y; wherein X represents (un) substituted C1-6 alkylene or (un) substituted phenylene; Y represents -A-B; wherein A represents (un) substituted C1-6 alkylene, O, S, NH, or (un) substituted C1-6 alkylene imino; B represents hydrogen, amino, amidino, acylimidoyl, (un) substituted imidazolyl, (un) protected bisphosphonomethyl, or (un)protected bisphosphonohydroxymethyl]. Also claimed are (i) medicinal and/or veterinary compns. containing I, in particular, metalloproteinase

inhibitors inhibiting matrix metalloproteinases and tumor necrosis factor- α (TNF- α) convertase and (ii) the use of I for the prevention or treatment of tissue degenerative diseases. These compds. have not only a high metalloproteinase inhibitory activity but also remarkably improved medicinal applicability (in vivo) (oral absorbability, etc.) and biol. activities and thus being useful as drugs. Thus, treatment of N α -tert-butoxycarbonyl-N ϵ ,N ϵ bis(benzyloxycarbonyl)-L-arginine-N-methylamide with 4 N HCl/EtOAc followed by condensation with 4-(p-phthalimidomethylphenyl)-3(RS)-tertbutoxycarbonyl-2(R)-isobutylbutyric acid, treatment with CF3CO2H, condensation with O-benzylhydroxylamine hydrochloride, and hydrogenolysis over 5% Pd-C gave Nα-[4-(hydroxyamino)-2(R)-isobutyl-3(RS)-(pphthalimidomethylbenzyl)succinyl]-L-arginine N-methylamine monoacetic acid salt (II). II showed IC50 of 2 nM against Matrix metalloproteinase MMP-3. Pharmaceutical formulations containing I, e.g. an ointment containing II, were described.

IT 228260-68-2P 228261-50-5P 228261-52-7P 228261-56-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of N-[4-(hydroxyamino) succinyl] amino acid amide derivs. as metalloproteinase tumor necrosis factor- α convertase inhibitors)

RN 228260-68-2 HCAPLUS

CN Butanediamide, N1-[(1S)-1-[[[2-(dimethylamino)ethyl]amino]carbonyl]-5-[(1-iminoethyl)amino]pentyl]-N4-hydroxy-2-(2-methylpropyl)-3-(3-phenylpropyl)-, (2R)-, diacetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 228260-67-1 CMF C29 H50 N6 O4

Absolute stereochemistry.

CM 2

CRN 64-19-7 CMF C2 H4 O2

RN 228261-50-5 HCAPLUS

CN Butanediamide, N-[(1S)-1-[[4-(aminomethyl)phenyl]methyl]-2-[[2-(dimethylamino)ethyl]amino]-2-oxoethyl]-N'-hydroxy-2,3-bis(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 228261-52-7 HCAPLUS

CN Butanediamide, N-[(1S)-2-[[2-(dimethylamino)ethyl]amino]-1-[[4-[[(1-iminoethyl)imino]methyl]phenyl]methyl]-2-oxoethyl]-N'-hydroxy-2,3-bis(2-methylpropyl)-, (2R)-, diacetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 228261-51-6 CMF C28 H46 N6 O4

Absolute stereochemistry.

Double bond geometry unknown.

CM 2

CRN 64-19-7 CMF C2 H4 O2

RN 228261-56-1 HCAPLUS

CN Butanediamide, 2-[3-(4-aminophenyl)propyl]-N4-[(1S)-1-[[[2-(dimethylamino)ethyl]amino]carbonyl]-5-[(1-iminoethyl)amino]pentyl]-N1-hydroxy-3-(2-methylpropyl)-, (3R)-, triacetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 228261-55-0 CMF C29 H51 N7 O4

Absolute stereochemistry.

CM 2

CRN 64-19-7 CMF C2 H4 O2

O || HO-- C-- CH₃

REFERENCE COUNT:

THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 31 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

7

ACCESSION NUMBER:

1999:231223 HCAPLUS

DOCUMENT NUMBER:

130:252675

TITLE:

Process for the preparation of N-acyl-L-tryptophan

carboxamide derivatives as synthetic matrix

metalloprotease inhibitors

INVENTOR(S):

Levy, Daniel E.; Grobelny, Damian; Tang, Cho; Holme, Kevin R.; Galardy, Richard E.; Schultz, Gregory S.;

Nematalia, Asaad; Musser, John H.

PATENT ASSIGNEE(S):

SOURCE:

Glycomed Incorporated, USA; The University of Florida U.S., 46 pp., Cont.-in-part of U.S. Ser. No. 44,324.

CODEN: USXXAM

DOCUMENT TYPE:

LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

7

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE				
		~						
	Α	19990406	US 1994-184727	19940121				
	Α	19920519	US 1990-616021	19901121				
US 5183900	Α	19930202		19901121				
	Α	19930223		19910820				
	Α			19910820				
	AA	19930221	CA 1991-2096225	19911121				
US 5268384	Α	19931207	US 1992-817039	19920107				
US 5270326		19931214						
US 5696147	Α	19971209						
US 5773438	Α	19980630	US 1994-464927	19940605				
CA 2158760	AA	19950727	CA 1995-2158760 WO 1995-US783	19950120				
WO 9519965	A1	19950727	WO 1995-US783	19950120				
W: AU, CA,	JP							
RW: AT, BE,	CH, DE	, DK, ES, F	R, GB, GR, IE, IT, LU	, MC, NL, PT, SE				
AU 9516049	A1	19950808	AU 1995-16049	19950120				
EP 690841	A1	19960110	EP 1995-908086	19950120				
R: AT, BE,	CH, DE	, DK, ES, F	R, GB, GR, IE, IT, LI	, LU, MC, NL, PT, SE				
JP 09501183	T2	19970204	JP 1995-519668	19950120				
AU 9883118	A1	19990128	AU 1998-83118	19980904				
AU 9910003	A1	19990304	AU 1999-10003	19990104				
PRIORITY APPLN. INFO	.:		US 1990-616021 A1	19901120				
			US 1990-615798 A2	19901121				
			US 1991-747751 A1	19910820				
				19910820				
				19920107				
				19920512				
			US 1993-44324 A2	19930407				
			US 1990-477751 B2	19900209				
			US 1991-615798 A	19911121				
			US 1994-184727 A3	19940121				
			AU 1994-65542 A3					
			AU 1995-16049 A3	19950120				
				19950120				
OTHER SOURCE(S):	MA	RPAT 130:25	2675					

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

GΙ

A process for the preparation of N-acyl-L-tryptophan derivs. I [R1 = H, alkyl; AΒ R2 = H, alkyl, NHZ; Z = R11, COR11, CO2R11; R11 = alkyl; R1R2 = (CH2)p; p = 3-5; R3 = H, C1-4 alkyl; R4 = Me, fused or conjugated, (un) substituted bicycloarylmethylene; n = 0-2; X = OR5, NHR5, NR5R5, NH(CH2)q, M; R5 = 0independently H, (un) substituted alkyl, (un) substituted aryl, (un) substituted arylalkyl; q = 1-8; M = amino acid residue, amino acid amide residue, cyclic amino, heterocyclic amino; R6 = H, lower alkyl; R7 = H, lower alkyl, acyl] as synthetic mammalian matrix metalloprotease inhibitors are disclosed that are useful for treating or preventing diseases wherein said diseases are caused by unwanted mammalian matrix metalloprotease activity and include skin disorders, keratoconus, restenosis, rheumatoid arthritis, wounds, cancer, angiogenesis and shock. Thus, benzyl 4-methyl-2-oxopentanoate underwent Wittig reaction with Ph3P:CHCO2Me (100%), hydrogenation of the formed unsatd. diester (86%), peptide coupling of the obtained monoacid with H-Trp-NHMe.HCl and separation of diastereomers (83%), and reaction with NH2OH (56% and 72%), to give isomeric title compds. II and III. II inhibited 72 kD gelatinase with Ki

= 0.26 nM and 92 kD gelatinase with Ki = 0.22 nM. Procedures using II for the inhibition of angiogenesis, treatment of psoriasis, treatment of chronic dermal wounds, treatment of thioglycollate-induced peritonitis, antimetastasis activity, treatment of hypovolumic shock, and antirestenotic activity are also given.

IT 142880-36-2P 142880-37-3P 142880-75-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(process for preparation of N-acyl-L-tryptophan carboxamide derivs. as synthetic matrix metalloprotease inhibitors)

RN 142880-36-2 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 142880-37-3 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 142880-75-9 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1R)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-, (2S)- (9CI) (CA INDEX NAME)

IT 142880-38-4P 142880-62-4P 162550-05-2P 171347-80-1P 171347-81-2P 171347-82-3P 171347-83-4P 171347-85-6P 200959-08-6P 221622-65-7P 221622-69-1P 221622-71-5P 221622-75-9P 221622-77-1P 221622-82-8P 221622-83-9P 221622-86-2P 221622-94-2P 221622-97-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(process for preparation of N-acyl-L-tryptophan carboxamide derivs. as synthetic matrix metalloprotease inhibitors)

RN 142880-38-4 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1R)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 142880-62-4 HCAPLUS

CN Carbamic acid, [6-[[(2S)-2-[[(2S)-2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]amino]-3-(1H-indol-3-yl)-1-oxopropyl]amino]hexyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

RN 162550-05-2 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-[[3-(4-morpholinyl)propyl]amino]-2-oxoethyl]-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 171347-80-1 HCAPLUS

CN Butanediamide, N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-N4-(phenylmethoxy)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 171347-81-2 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-N4-(phenylmethyl)-, (2R)- (9CI) (CA INDEX NAME)

RN 171347-82-3 HCAPLUS

CN Butanediamide, N4-[(4-fluorophenyl)methyl]-N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 171347-83-4 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-N4-(methoxymethyl)-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 171347-85-6 HCAPLUS

CN Glycine, N-hydroxy-N-[(3R)-3-[[[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]amino]carbonyl]-5-methyl-1-oxohexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 200959-08-6 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-oxo-2-[[(1S)-1-phenylethyl]amino]ethyl]-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 221622-65-7 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-N1-methyl-2-(2-methylpropyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 221622-69-1 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1S)-2-[(2-hydroxyethyl)amino]-1-(1H-indol-3-ylmethyl)-2-oxoethyl]-2-(2-methylpropyl)- (9CI) (CA INDEX NAME)

RN 221622-71-5 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-oxo-2-(pentylamino)ethyl]-2-(2-methylpropyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 221622-75-9 HCAPLUS

CN Butanediamide, N1-[(1S)-2-(dodecylamino)-1-(1H-indol-3-ylmethyl)-2-oxoethyl]-N4-hydroxy-2-(2-methylpropyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 221622-77-1 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-oxo-2-[[(1S)-1-phenylethyl]amino]ethyl]-2-(2-methylpropyl)- (9CI) (CA INDEX NAME)

RN 221622-82-8 HCAPLUS

CN Butanediamide, N4-(acetyloxy)-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 221622-83-9 HCAPLUS

CN Butanediamide, N4-(benzoyloxy)-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 221622-86-2 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-[[2-(4-morpholinyl)ethyl]amino]-2-oxoethyl]-2-(2-methylpropyl)-, (2R)- (9CI) (CFINDEX NAME)

RN 221622-94-2 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-3-(phenylmethyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 221622-97-5 HCAPLUS

CN Propanoic acid, 2,2-dimethyl-, [hydroxy[(3R)-3-[[[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]amino]carbonyl]-5-methyl-1-oxohexyl]amino]methyl ester (9CI) (CA INDEX NAME)

IT 171347-98-1P 171348-01-9P 171348-03-1P

171348-04-2P 221622-96-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(process for preparation of N-acyl-L-tryptophan carboxamide derivs. as synthetic matrix metalloprotease inhibitors)

RN 171347-98-1 HCAPLUS

CN Butanediamide, N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-[[3-(4-morpholinyl)propyl]amino]-2-oxoethyl]-2-(2-methylpropyl)-N4-(phenylmethoxy)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 171348-01-9 HCAPLUS

CN Butanediamide, N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-N4-(phenylmethoxy)-N4-(phenylmethyl)-, (2R)-(9CI) (CA INDEX NAME)

RN 171348-03-1 HCAPLUS

CN Propanoic acid, 2,2-dimethyl-, [[(3R)-3-[[[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]amino]carbonyl]-5-methyl-1-oxohexyl](phenylmethoxy)amino]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 171348-04-2 HCAPLUS

CN Glycine, N-[(3R)-3-[[[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]amino]carbonyl]-5-methyl-1-oxohexyl]-N-(phenylmethoxy)-, phenylmethyl ester (9CI) (CA INDEX NAME)

RN 221622-96-4 HCAPLUS

CN Butanediamide, N4-[(4-fluorophenyl)methyl]-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-N4-(phenylmethoxy)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT:

21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 32 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1999:77667 HCAPLUS

DOCUMENT NUMBER:

130:136300

TITLE:

Methods for the preparation of artificial cellular tissue using matrix metalloproteinase inhibitors

INVENTOR(S):

Wolowacz, Richard; Wolowacz, Sorrel; Sheridan, Julie

Marie

PATENT ASSIGNEE(S):

Smith & Nephew PLC, UK PCT Int. Appl., 28 pp.

SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

	PAT	ENT I	NO.		KII	MD 1	DATE			A	PPLI	CATI	ON NO). I	DATE			
										-					- -			
	WO	9903	979		A:	1 :	1999	0128		W	199	98 - GI	3214′	7 :	1998(717		
		W:	AL,	AM,	AT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CU,	CZ,	DE,
			DK,	EE,	ES,	FI,	GB,	GE,	GH,	GM,	HR,	ΗU,	ID,	IL,	IS,	JP,	ΚE,	KG,
	KP, K			KR,	KΖ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	MD,	MG,	MK,	MN,	MW,	MX,
	NO, N			NZ,	PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	ТJ,	ΤM,	TR,	TT,
	UA, U			UG,	US,	UΖ,	VN,	YU,	ZW,	AM,	ΑZ,	BY,	KG,	KΖ,	MD,	RU,	ТJ,	TM
		RW:	GH,	GM,	KΕ,	LS,	MW,	SD,	SZ,	UG,	ZW,	ΑT,	BE,	CH,	CY,	DE,	DK,	ES,
			FΙ,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,	CF,	CG,	CI,
			CM,	GΑ,	GN,	GW,	ML,	MR,	ΝE,	SN,	TD,	TG						
	ΑU	9884	514		A:	1 :	1999	0210		Αl	J 199	98-84	1514	-	1998	717		
PRIO	RITY	APP	LN.	INFO	. :					GB 1:	997-	14936	5		19970	717		
									1	WO 1:	998-0	GB214	17		1998	0717		
				-				_							/			

AB There is disclosed the use of matrix metalloproteinase (MMP) inhibitors, e.g. collagenase, stromelysin, or gelatinase inhibitors in the production of tissue equivalent. The inhibitors are used in particular to inhibit MMPs present in animal serum used in the production technique, thereby increasing collagen deposition. Tissue culture media and extracted animal serum containing a

supplemented MMP inhibitor are also disclosed. Polylactic acid yarns seeded with fibroblasts of human fetal foreskin were cultured with media supplemented with doxycycline. Increased collagen content was observed in

the test samples compared to control (lacking doxycycline).

IT 142880-36-2, Galardin

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(as inhibitor; matrix metalloproteinase inhibitors in preparation of artificial cellular tissue)

RN 142880-36-2 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT:

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 33 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

5

ACCESSION NUMBER:

1998:786799 HCAPLUS

Correction of: 1998:682232

DOCUMENT NUMBER:

129:343729

Correction of: 129:290443

TITLE:

Preparation of Hydroxamic acids substituted by

heterocycles as TNF production inhibitors

INVENTOR(S):

Bird, Thomas Geoffrey Colerick

PATENT ASSIGNEE(S):

Zeneca Limited, UK; Zeneca Pharma S.A.

SOURCE:

PCT Int. Appl., 61 pp.

CODEN: PIXXD2

DOCUMENT TYPE: LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT:

Englis

PATENT INFORMATION:

PATENT NO.	KIND DATE	APPLICATION NO. DATE
WO 9843959	AI 19981008	WO 1998-GB910 19980325
W: AL, AM,	AT, AU, AZ, BA,	BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
DK, EE,	ES, FI, GB, GE,	GH, GM, GW, HU, ID, IL, IS, JP, KE, KG,
KP, KR,	KZ, LC, LK, LR,	LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,
NO, NZ,	PL, PT, RO, RU,	SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
UA, UG,	US, UZ, VN, YU,	ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM,	KE, LS, MW, SD,	SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI,
FR, GB,	GR, IE, IT, LU,	MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM,
GA, GN,	ML, MR, NE, SN,	TD, TG
AU 9868432	A1 19981022	AU 1998-68432 19980325
EP 971895	A1 20000119	EP 1998-913907 19980325
R: AT, BE,	CH, DE, DK, ES,	FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, FI		

T2 20011009 JP 1998-541286 19980325 JP 2001518090 19990924 US 6251913 B1 20010626 US 1999-381836 20020404 US 2001-814119 20010322 US 2002040002 Α1 EP 1997-400725 Α 19970328 PRIORITY APPLN. INFO .: A 19980325 WO 1998-GB910 A1 19990924 US 1999-381836

MARPAT 129:343729

OTHER SOURCE(S):

GT

Title compds. [I; wherein: n is 1 to 6; Het is a nitrogen containing ring AB fused to the benzene ring on two adjacent carbon atoms to form a bicyclic ring system which ring system may be optionally substituted; R1 is hydrogen, C1-8alkyl, C2-6alkenyl, C2-6alkynyl, C3-8cycloalkyl, aryl, heteroaryl, heterocyclyl, arylC1-6alkyl, heteroarylC1-6alkyl, heterocyclylC1-6alkyl or C3-8cycloalkylC1-6alkyl; R2 is C1-6alkyl, C2-6alkenyl, arylC1-6alkyl, heteroarylC1-6alkyl or the side-chain of a naturally occurring amino acid; R3 is hydrogen, C1-6alkyl, C3-8cycloalkyl, C4-8cycloalkenyl, arylC1-6alkyl, heteroarylC1-6alkyl or heterocyclylC1-6alkyl; R4 is hydrogen or C1-6alkyl; or R3 and R4 together with the nitrogen atom to which they are joined form a heterocyclic ring; wherein any group or ring, in R1-R4, is optionally substituted], stereoisomers, pharmaceutically acceptable salts, and in vivo hydrolyzable esters thereof, are prepared and described as inhibitors of TNF production inhibitors.

Ι

IT 215606-12-5P 215606-21-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of hydroxamic acids substituted by heterocycles as TNF production

inhibitors)

RN 215606-12-5 HCAPLUS

CN Butanediamide, 2-[(1,2-dihydro-1-methyl-2-oxo-6-quinolinyl)methoxy]-N4[(1S)-1-[[[2-(dimethylamino)ethyl]amino]carbonyl]-2,2-dimethylpropyl]-N1hydroxy-3-(2-methylpropyl)-, (2S,3R)- (9CI) (CA INDEX NAME)

RN 215606-21-6 HCAPLUS

CN Butanediamide, N1-[(1S)-1-[[[2-(dimethylamino)ethyl]amino]carbonyl]-2,2-dimethylpropyl]-N4-hydroxy-2-(2-methylpropyl)-3-(8-quinolinylmethoxy)-, (2R,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L20 ANSWER 34 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1998:709044 HCAPLUS

DOCUMENT NUMBER:

129:331045

TITLE:

Preparation of amino acid derivatives which inhibit

extracellular matrix metalloproteinase and $\textsc{TNF-}\alpha$

release

INVENTOR(S):

Jeanpetit, Christian; Pringent, Didier; Settembre,

Pierre-Andre; Trancart, Marie-Michele

PATENT ASSIGNEE(S): SOURCE:

Laboratoires Jacques Logeais, Fr. PCT Int. Appl., 106 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

French

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT	NO.		KI	ND 1	DATE			A.	PPLI	CATI	ON NC). (DATE			
				-, -				_								
WO 984		A	1	1998	1029		W	0 19	98-F	R801		1998	0421			
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	DK,	EE,	ES,	FI,	GB,	GE,	GH,	GM,	GW,	HU,	ID,	IL,	IS,	JP,	KE,	KG,
	KΡ,	KR,	ΚZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	MD,	MG,	MK,	MN,	MW,	MX,

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NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
             UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
             CM, GA, GN, ML, MR, NE, SN, TD, TG
     FR 2762315
                            19981023
                                            FR 1997-4971
                                                              19970422
                       Α1
     FR 2762315
                       В1
                            19990528
     AU 9875346
                            19981113
                                            AU 1998-75346
                                                              19980421
                       Α1
                                            EP 1998-922850
     EP 977730
                       A1
                            20000209
                                                              19980421
    EP 977730
                       В1
                            20030312
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
     AT 234278
                       E
                            20030315
                                            AT 1998-922850
                                                              19980421
     ES 2194319
                                            ES 1998-922850
                                                              19980421
                       Т3
                            20031116
                            19990209
                                            ZA 1998-3390
     ZA 9803390
                                                              19980422
                       Α
                            20020205
                                            US 1999-403037
     US 6344457
                       B1
                                                              19991217
                                         FR 1997-4971
PRIORITY APPLN. INFO.:
                                                          Α
                                                              19970422
                                         WO 1998-FR801
                                                              19980421
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OTHER SOURCE(S):

MARPAT 129:331045

Amino acid derivs. YCHR2CR1(OH)CO-AA-R3 [Y = CONHOH, SH, N(OH)CHO, P(O)R5OR4, where R4 = H, alkyl; R5 = (un)substituted 1,8-naphthalenedicarboximido; R1 = alkyl or cycloalkyl chain optionally containing a heteroatom, (un)substituted phenoxyalkyl or phenylalkyl, heteroarylalkyl; R2 = H, alkyl, alkylidene, OH, alkoxy, benzyloxy, hydroxymethyl, alkoxymethyl, arylalkyl, aryloxymethyl, arylthiomethyl, heteroarylthiomethyl, phthalimidoalkyl, alkoxycarbonylmethyl, benzyloxycarbonylmethyl, acetylmethyl; AA represents an amino acid residue or sequence; R3 = substituted alkylamino] were prepared as inhibitors of extracellular matrix metalloproteinase and TNF-α release. Thus, (S,S)-HONHCOCHMeC(OH)(Bu-i)CO-Tyr(Me)-NHMe, prepared by a multistep procedure, showed CI50 = 1 μM for inhibition of TNF.

IT 215310-95-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of amino acid derivs. which inhibit extracellular matrix metalloproteinase and $\text{TNF-}\alpha$ release)

RN 215310-95-5 HCAPLUS

CN Butanediamide, N4,2-dihydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-3-methyl-2-(2-methylpropyl)-, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT:

6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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HCAPLUS COPYRIGHT 2004 ACS on STN
L20 ANSWER 35 OF 63
                         1998:424117 HCAPLUS
ACCESSION NUMBER:
                         129:113523
DOCUMENT NUMBER:
                         Use of matrix metalloproteinase inhibitors for
TITLE:
                         treating neurological disorders and promoting wound
                         healing
                         Bocan, Thomas Michael Andrew; Boxer, Peter Alan;
INVENTOR(S):
                         Peterson, Joseph Thomas, Jr.; Schrier, Denis; White,
                         Andrew David
                         Warner-Lambert Co., USA; Bocan, Thomas Michael Andrew;
PATENT ASSIGNEE(S):
                         Boxer, Peter Alan; Peterson, Joseph Thomas, Jr.;
                         Schrier, Denis; White, Andrew David
                         PCT Int. Appl., 163 pp.
SOURCE:
                         CODEN: PIXXD2
DOCUMENT TYPE:
                         Patent
                         English
LANGUAGE:
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
     PATENT NO.
                                          APPLICATION NO. DATE
                      KIND DATE
                     ____
                            19980625
                                           WO 1997-US21532 19971121
     WO 9826773
                      A1
         W: AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, HU, ID, IL, IS, JP,
             KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI,
             SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU,
             TJ, TM
         RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,
             GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,
             GN, ML, MR, NE, SN, TD, TG
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                            20010809
     AU 737117
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                                                             19971121
     EP 946166
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                       T2
                            20010605
                                           JP 1998-527715
                                                             19971121
     JP 2001507342
                            20010629
                                           NZ 1997-334925
                                                             19971121
     NZ 334925
                       Ά
     EP 1366765
                       Α1
                            20031203
                                           EP 2003-18081
                                                             19971121
             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, AL
                                                             19971121
     AT 259640
                       Ε
                            20040315
                                            AT 1997-949584
     ZA 9711279
                       Α
                            19980623
                                            ZA 1997-11279
                                                             19971215
     US 6340709
                       В1
                            20020122
                                           US 1999-269123
                                                             19990319
                                         US 1996-32753P P 19961217
PRIORITY APPLN. INFO.:
                                         EP 1997-949584
                                                          A3 19971121
                                         WO 1997-US21532 W 19971121
OTHER SOURCE(S):
                         MARPAT 129:113523
    Matrix metalloproteinase inhibitors 4-RC6H4SO2NHCHR1COR2 [R =
     (un) substituted Ph; R1 = alkyl, phenylalkyl, phenyl; R2 = OH, alkoxy,
     NHOH] and 4-RC6H4C(:NR3)CR4R5CR6R7COR8 [R3 = (un)substituted OH, NH2;
     R4-R7 = H, F, (un)substituted alkyl; R8 = OH, SH] are useful for
     preventing and treating neurol. disorders, especially Alzheimer's,
huntington's,
     and Parkinson's diease and amyotropic lateral sclerosis, and in promoting
     wound healing. IC50 for matrix metalloproteinase inhibition are reported
     for a number of compds. Formulations containing (R)-4-(4-
     {\tt NCC6H4)\,C6H4SO2NHCH\,(CO2H)\,CH2Ph}\,,\quad {\tt (S)-4-(4-H2NC6H4)\,C6H4SO2NHCH\,(CO2H)\,CH2C6H4OE}
     t-3, and 4-(4-BrC6H4)C6H4SO2NHCH(CO2H)CHMe2 are reported.
```

106314-87-8, U24522 142880-36-2, Galardin

ΤТ

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(use of matrix metalloproteinase inhibitors for treating neurol.

disorders and promoting wound healing)

106314-87-8 HCAPLUS RN

L-Phenylalaninamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-CN oxopentyl]-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

142880-36-2 HCAPLUS RN

Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-CN 2-oxoethyl]-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT:

THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS 13 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 36 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1998:402296 HCAPLUS

DOCUMENT NUMBER:

129:76499

TITLE:

Method for treating and preventing heart failure and

ventricular dilation

INVENTOR(S):

Peterson, Joseph T., Jr.

PATENT ASSIGNEE(S): SOURCE:

Warner-Lambert Co., USA PCT Int. Appl., 178 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.

KIND DATE APPLICATION NO. DATE

```
WO 1997-US21934 19971202
     WO 9825597
                            19980618
     WO 9825597
                       Α3
                            20001012
             AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, HU, ID, IL, IS, JP,
             KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI,
             SK, SL, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,
             GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,
             GN, ML, MR, NE, SN, TD, TG
                                            AU 1998-55906
     AU 9855906
                       Α1
                            19980703
                                                              19971202
     AU 741768
                       B2
                            20011206
     BR 9714385
                                            BR 1997-14385
                       Α
                            20000516
                                                              19971202
     EP 1028716
                                            EP 1997-952246
                                                              19971202
                       Α1
                            20000823
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
                                            NZ 1997-334897
     NZ 334897
                       Α
                            20010223
                                                              19971202
                                            JP 1998-526758
                            20011218
     JP 2001526631
                       T2
                                                              19971202
                                            ZA 1997-11004
     ZA 9711004
                            19981005
                                                              19971208
                       Α
                                            US 1997-987167
     US 5948780
                            19990907
                                                              19971208
                       Α
     NO 9902769
                            19990809
                                            NO 1999-2769
                                                              19990608
                       Α
                                                              19961209
PRIORITY APPLN. INFO .:
                                         US 1996-32631P
                                         WO 1997-US21934 W
                                                             19971202
```

OTHER SOURCE(S):

MARPAT 129:76499

AB Matrix metalloproteinase inhibitors are useful for preventing and treating heart failure, and ventricular dilation in mammals. Thus,

2-(4'-bromobiphenyl-4-sulfonylamino)-3-methylbutyric acid was effective in protecting pigs in the pacing-induced heart failure model.

IT 106314-87-8, U24522 142880-36-2, Galardin

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(use of matrix metalloproteinase inhibitors in treating heart failure and ventricular dilation)

RN 106314-87-8 HCAPLUS

CN L-Phenylalaninamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 142880-36-2 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

L20 ANSWER 37 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1998:394241 HCAPLUS

DOCUMENT NUMBER:

129:62957

TITLE:

Inhibitors of invasive tissue remodelling for use as

contraceptives and antitumor agents

INVENTOR(S):

Lund, Leif Roge; Dano, Keld; Stephens, Ross; Brunner, Nils; Solberg, Helene; Holst-Hansen, Claus; Nielsen,

John Romer

PATENT ASSIGNEE(S):

Fonden Til Fremme Af Eksperimentel Cancerforskning, Den.; Dano, Keld; Stephens, Ross; Brunner, Nils; Solberg, Helene; Holst-Hansen, Claus; Nielsen, John

Patent

SOURCE:

PCT Int. Appl., 113 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

English LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

		CENT 1				ND	DATE					CATIO		o. :	DATE			
		9824				1	1998	0611							1997	1208		
		W:	AL,	AM,	AT,	ΑT,	AU,	ΑZ,	ΒA,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CU,	CZ,
			CZ,	DE,	DE,	DK,	DK,	EE,	EE,	ES,	FΙ,	FI,	ĢΒ,	GE,	GH,	HU,	ID,	ΙL,
			IS,	JP,	KΕ,	KG,	KΡ,	KR,	KΖ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	MD,	MG,
			MK,	MN,	MW,	MX,	NO,	NZ,	ΡL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SK,
			SL,	ТJ,	TM,	TR,	TT,	UA,	UG,	US,	UŻ,	VN,	YU,	ZW,	AM,	ΑŻ,	BY,	KG,
			KZ,	MD,	RU,	ТJ,	TM											
		RW:	GH,	KE,	LS,	MW,	SD,	SZ,	UG,	ZW,	ΑT,	BE,	CH,	DE,	DK,	ES,	FΙ,	FR,
			GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,
							SN,											
	ΑU	9851	876		A:	1	1998	0629		A	J 19	98-5	1876		1997	1208		
	ΕP	9427	46		A:	1	1999	0922		E	P 19	97-9	4674	6	1997	1208		
		R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	ΝL,	SE,	MC,	PT,
			ΙE,	FI														
	US	2002	0990	04	A	2002	0725		U	S 20	01-9	9563	6	2001	1129			
PRIO	RIT	Y APP	LN.	INFO	. :				DK 1:	996-	1402		Α	1996	1206			
									1	WO 1:	997-	DK55	5	W	1997	1208		
									1	US 1	999-	3194	64	B1	1999	0827		
AB	The	- inv	entid	on p	erta	ins	to n	ovel	met:	hods	for	pre	vent:	ing	or a	rres	ting	

The invention pertains to novel methods for preventing or arrestin invasive remodelling in mammals by utilising a combination of in vivo inhibition of plasmin and in vivo inhibition of certain other proteolytic enzymes, notably metalloproteases. The method can e.g. be used as a novel alternative to current methods of contraception as well as antifungal and antibacterial treatment. The preferred embodiments relate to treatment

and prevention of neoplastic diseases by use of these combinations. Further, the invention relates to novel compns. which comprises a plasmin inhibitor in admixt. with an inhibitor of another proteolytic enzyme, preferably an inhibitor of a metalloprotease.

IT 142880-36-2, Galardin

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(inhibitors of invasive tissue remodelling for use as contraceptives and antitumor agents)

RN 142880-36-2 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT:

THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 38 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

7

ACCESSION NUMBER:

1998:219789 HCAPLUS

DOCUMENT NUMBER:

128:283080

TITLE:

Preparation of hydroxamic acid derivatives for the

suppression of TNF release and for treatment of

autoimmune and inflammatory diseases

INVENTOR(S):

Kottirsch, Georg; Neumann, Ulf

PATENT ASSIGNEE(S):

Novartis A.-G., Switz.; Kottirsch, Georg; Neumann, Ulf

PCT Int. Appl., 34 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

SOURCE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT	NO.		KI	ND 1	DATE			A	PPLI	CATI	ON NC	o. 1	DATE			
				'				_					-			
WO 9814	424		Α	1	1998	0409		Mo	199	97-E	P537	6 :	19970	0930		
W:	AL,	AM,	ΑT,	AU,	AZ,	BA,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CU,	CZ,	DE,
	DK, EE, ES, FI,					GE,	GH,	HU,	ID,	IL,	IS,	JP,	KΕ,	KG,	ΚP,	KR,
	KZ, LC, LK, LR, LS, LT, I						LU,	LV,	MD,	MG,	MK,	MN,	MW,	MX,	NO,	NΖ,
	PL, PT, RO, RU, SD, SE, S						SG,	SI,	SK,	SL,	TJ,	TM,	TR,	TT,	UA,	UG,
	US,	UΖ,	VN,	YU,	ZW,	AM,	ΑZ,	BY,	KG,	ΚZ,	MD,	RU,	ΤĴ,	TM .		
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	GN,	ML,	MR,	ΝE,	SN,	TD,	TG									
AU 9747068			Α	1	1998	0424		A	U 19:	97-4	7068		19970	0930		
AU 7260	65		B	2 :	2000	1026										

EP S	929517 929517			A1	1 19	990	0721		EI	Ρ	1997	-90	9339	9	1997	0930		
EP S	929517	7		В1	20	020	0612											
					DE, I	K,	ES,	FR,	GB,	G	R, I	Τ,	LI,	LU,	NL,	SE,	PT,	ΙE,
			FΙ,															
BR S	971225	55		Α	19	990	0824		BI	?	1997	-12	2255		1997	0930		
CN 3	123244	17		Α	19	99:	1020		Cl	N	1997	-19	9851	l	1997	930		
CN :	110180	7		В	20	030	0219											
JP 2	200050	833	8	T^2	2 20	000	0704		JI	Б	1998	-51	L623	5	1997	0930		
JP 3	344489	8		B2	2 20	030	0908											
NZ 3	334908	3		Α	20	00	1027		NZ	Z	1997	-33	34908	3	1997	0930		
AT 2	219050)		E	20	020	0615		A.	Γ	1997	-90	9339	9	1997	0930		
PT :	929517	7		T	20	02	1031		Ρ.	Г	1997	-90	9339	9	1997	0930	*	
ES 2	217875	59		T^3	3 20	03	0101		ES	5	1997	-9(9339	9	1997	0930		
RU :	219613	31		C2	2 20	036	0110		RU	J	1999	-10	8792	2	1997	0930		
ZA S	970880	0 0		. A	19	981	0402		$\mathbf{Z}I$	Ą	1997	-88	300		1997	1001		
NO S	990155	59		Α	19	991	0330		NO)	1999	-15	559		1999	0330		
KR :	200004	881	1	A	20	00	0725		KI	R	1999	-70	280	5	1999	0401		
HK :	102163	37 -		A.	L 20	03	0502		HI	K	2000	-10	00370)	2000	0120		
US :	200203	804	5	A:	L 20	02	0328		US	S	2001	-97	7325!	5	2001	1009		
US (650098	33		B	2 20	02	1231							•				
PRIORITY	APPLN	J. I	NFO.	. :				C	B 19	99	6-20	572	2	Α	1996	1002		
								C	B 19	99	7-66	67		Α	1997	0402		
											7-EP				1997			
										99	9-26	986	57	A1	1999	0401		
OTHED COL	TIDCE (C	: 1:			MARDZ	T .	128.	28308	۱۸									

OTHER SOURCE(S):

MARPAT 128:283080

GΙ

3-Aza-4-oxo-6-(oxymethyl)heptane 1,7-dioic acid (7-N-hydroxy)diamide and AΒ related compds. [I; R1 = A[O(CHR5)n]mOCH2; n = 1-4; m = 0-3; R5 = H, (substituted)alkyl, alkenyl, (substituted)aryl, etc.; A = H, alkyl, aryl, (aryl)alkyl, (aryl)carbonyl, (alkyl)carbonyl; R2 = alkyl, alkenyl, (substituted)cycloalkyl, (substituted)aryl; R3 = (substituted)alkyl, (substituted)aryl, indolylmethyl; R4 = Me, pyridyl, XY; X = morpholino, pyridyl, aryl; Y = C1-12 alkylene in which up to four of the methylene units are optionally replaced with CO, NH, SO2 or O] are claimed. For example, hydroxamic acid II is prepared from the starting materials of (E)-1,4-dibromobut-2-ene, diethylene glycol monomethyl ether, isocaproic acid, H-Phe-NHMe. The present compds. are useful in pharmaceuticals, such as in the suppression of TNF release (a range of IC50 values of 50 nM to 5 µM for title compds.), and in the treatment of inflammatory diseases (title compds. show dose dependent inhibition of collagenase at concns. below 10 nM).

IT 205806-93-5P 205806-95-7P 205807-08-5P 205807-28-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of hydroxamic acids for suppression of TNF release and for treatment of autoimmune and inflammatory diseases)

RN 205806-93-5 HCAPLUS

CN Butanediamide, N1-hydroxy-2-[[2-(2-methoxyethoxy)ethoxy]methyl]-N4-[2-[[2-[[4-methylphenyl)sulfonyl]amino]ethyl]amino]-2-oxo-1-(phenylmethyl)ethyl]-3-(2-methylpropyl)-, [2R-[2R*,3R*,4(S*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 205806-95-7 HCAPLUS

CN L-Alaninamide, N-[(2R)-2-[(1R)-2-(hydroxyamino)-1-[[2-(2-methoxyethoxy)ethoxy]methyl]-2-oxoethyl]-4-methyl-1-oxopentyl]-L-phenylalanyl-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 205807-08-5 HCAPLUS

CN Butanediamide, N1-hydroxy-N4-[1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-[[2-(2-methoxyethoxy)ethoxy]methyl]-3-(2-methylpropyl)-,
[2R-[2R*,3R*,4(S*)]]- (9CI) (CA INDEX NAME)

RN 205807-28-9 HCAPLUS

CN Butanediamide, 2-[[2-(cyclohexyloxy)ethoxy]methyl]-N1-hydroxy-N4-[1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-3-(2-methylpropyl)-,
[2R-[2R*,3R*,4(S*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT:

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 39 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

.5

ACCESSION NUMBER:

1998:161082 HCAPLUS

DOCUMENT NUMBER:

128:205148

TITLE:

Preparation of peptide sulfonamides as inhibitors of

tumor necrosis factor

INVENTOR(S):

Barlaam, Bernard Christophe

PATENT ASSIGNEE(S): SOURCE:

Zeneca Limited, Fr. PCT Int. Appl., 70 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

. 1

PATENT INFORMATION:

PAT	PATENT NO. KIND					DATE			A.	PPLI	CATI	N NC	ο.	DATE			
									_								
WO	9807	742		A:	1	1998	0226		W	0.19	97-G	B222.	2	1997	0819		
	W:	AL,	AM,	ΑT,	ΑU,	ΑZ,	BB,	ВG,	BR,	BY,	CA,	CH,	CN,	CU,	CZ,	DE,	DK,
		EE,	ES,	FI,	GB,	GE,	GH,	ΗÜ,	IL,	IS,	JP,	KΕ,	KG,	ΚP,	KR,	ΚZ,	LC,
		LK,	LR,	LS,	LT,	LU,	LV,	MD,	MG,	MN,	MW,	MX,	NO,	NZ,	PL,	PΤ,	RO,
		RU,	SD,	SE,	SG,	SI,	SK,	SL,	ŢJ,	TM,	TR,	TT,	UA,	UG,	US,	UΖ,	VN,
		YU,	ZW,	AM,	ΑZ,	BY,	KG,	ΚZ,	MD,	RU,	ΤJ,	TM					
	RW:	GH,	KE,	LS,	MW,	SD,	SZ,	ŪĠ,	ZW,	AT,	ΒE,	CH,	DE,	DK,	ES,	FΙ,	FR,

GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9740217 A1 19980306 AU 1997-40217 19970819 ZA 9707580 19990217 ZA 1997-7580 19970822 Ά FR 1996-1815 PRIORITY APPLN. INFO.: 19960823 Α FR 1996-2031 19960925 Α EP 1996-401815 19960823 Α EP 1996-402031 Α 19960925 WO 1997-GB2222 19970819

OTHER SOURCE(S): MARPAT 128:205148

AB Peptide sulfonamides HONHCOCH(NHSO2R1)CHR2CONHCHR3CONR4R5 (R1 = aryl, heterocyclyl, heteroaryl; R2 = H, alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, heterocyclyl, aryl-, heteroaryl-, heterocyclyl- or cycloalkylalkyl; R3 = alkyl, alkenyl, aryl, alkyl, heteroarylalkyl or the side-chain of a naturally occurring amino acid; R4 = H, alkyl, cycloalkyl, cycloalkenyl, aryl-, heteroaryl- or heterocyclylalkyl; R5 = H, alkyl or R4R5N = heterocyclyl; any group or ring in R1-R5 is optionally substituted) or their pharmaceutically acceptable salts or in vivo hydrolyzable esters were prepared as inhibitors of the production of tumor necrosis factor and/or one or more matrix metalloproteinase enzymes.

Thus, N2-[4-(hydroxyamino)-2R-isobutyl-3S-benzenesulfonylaminosuccinyl]-L-leucine-N1-methylamide was prepared via sequential benzenesulfonylation, deprotection, and hydroxylamination of intermediate N2-[2R-isobutyl-3S-amino-4-tert-butyloxysuccinyl]-L-leucine-N1-methylamide.

IT 204125-87-1P

RN

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of peptide sulfonamides as inhibitors of tumor necrosis factor) 204125-87-1 HCAPLUS

CN L-Valinamide, (3R)-N-hydroxy-3-(2-methylpropyl)-N2-(8-quinolinylsulfonyl)L-α-asparaginyl-N-[2-(dimethylamino)ethyl]-3-methyl- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT:

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 40 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1997:756963 HCAPLUS

DOCUMENT NUMBER:

127:359105

TITLE:

Preparation of sulfur-containing aminoacyl hydroxamic acid derivatives as tumor necrosis factor and matrix

metalloproteinase inhibitors

INVENTOR(S): Bird, Thomas Geoffrey Colerick; Barlaam, Bernard

Christophe; Lambert, Christine Marie Paul

PATENT ASSIGNEE(S): Zeneca Limited, Fr.

PCT Int. Appl., 72 pp. SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

GI

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT	NO.	KI	ND I	DATE				PPLI				DATE			
 ₩∩ 9742	168	Δ.	· 1 '	 1997	 1113			 0 19				1997	 0429		
	AL, AM													DE.	DK.
	EE, ES					•					•	•		•	•
	LS, LT	LU,	LV,	MD,	MG,	MX,	NO,	NZ,	PL,	PT,	RO,	RU,	SD,	SE,	SG,
	SI, SK	TJ,	TM,	TR,	TT,	UA,	UG,	US,	UZ,	VN,	YU,	AM,	ΑZ,	BY,	KG,
	KZ, MD	•	•												
RW:	RW: GH, KE, LS GR, IE, IT						-			•	-			-	
	•		-		NЬ,	PT,	SE,	BF,	CF,	CG,	CI,	CM,	GA,	GN,	ML,
ΔII 9726	MR, NE				1126		Δ	II 19	97-2	6454		1997	0429		
	842							A 19							
PRIORITY APP								996-							
								996-							
]	FR 1	996-	2032		Α	1996	0925		
						•		996-							
								997-0	GB11	54	W	1997	0429		
OTHER SOURCE	(S):		MARI	PAT :	127:	3591	05								

Title compds. I [R1 = aryl, aryl-C1-6 alkyl, heteroaryl, heteroaryl-C1-6 alkyl; R2 = H, C1-8 alkyl, C2-6 alkenyl, C2-6 alkynyl, C3-8 cycloalkyl, AB heteroaryl, heterocyclyl, aryl-C1-6 alkyl, heteroaryl-C1-6 alkyl, heterocyclyl-C1-6 alkyl, C3-8 cycloalkyl-C1-6 alkyl; R3 = C1-6 alkyl, C2-6 alkenyl, aryl, C1-6 alkyl, heteroaryl-C1-6 alkyl, naturally occurring

amino acid side chain; R4 = H, C1-6 alkyl, C3-8 cycloalkyl, C4-8 cycloalkenyl, aryl-C1-6 alkyl, heteroaryl-C1-6 alkyl, heterocyclyl-C1-6 alkyl; R5 = H, C1-6 alkyl; NR4R5 = heterocyclic ring; wherein any group or ring in R1-R5 may be (un)substituted] or pharmaceutically acceptable salts or in vivo hydrolyzable esters thereof, are described as inhibitors of the production of tumor necrosis factor and/or one or more matrix metalloproteinase enzymes. Compns. containing I and their preparation are also described. Thus, deprotonation of 3.45 g (2R)-isobutyl-1,4-butanedioic acid 4-tert-Bu ester and reaction with 4.2 g Ph2S2 gave 2.3 g (2S,3S)-adduct II, along with 2.2 g of the corresponding (2S,3R)-adduct. Coupling of 2.75 g II with 1.41 g L-tert-leucine methylamide gave 3.0 g adduct III (R = OCMe3), which underwent deprotection with CF3CO2H and hydroxyamidation with hydroxylamine hydrochloride to give desired title compound III (R = NHOH).

IT 198421-34-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of sulfur-containing aminoacyl hydroxamic acid derivs. as tumor necrosis factor and matrix metalloproteinase inhibitors)

RN 198421-34-0 HCAPLUS

CN Butanediamide, N1-[1-[[[2-(dimethylamino)ethyl]amino]carbonyl]-2,2-dimethylpropyl]-N4-hydroxy-2-(2-methylpropyl)-3-[(1,2,3,4-tetrahydro-1-methyl-2-oxo-6-quinolinyl)thio]-, [2S-[1(R*),2R*,3R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L20 ANSWER 41 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1997:499085 HCAPLUS

DOCUMENT NUMBER:

127:180935

TITLE:

Inhibition of skin photoaging by inhibitors of matrix

metalloproteinase production

INVENTOR(S):

Voorhees, John J.; Fisher, Gary J.

PATENT ASSIGNEE(S):

University of Michigan, USA

SOURCE:

PCT Int. Appl., 24 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9725969	A1	19970724	WO 1997-US791	19970117

```
AU, BB, BR, BY, CA, CN, CZ, EE, GE, HU, IS, JP, KP, KR, LT, MK,
         MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
                        Α
                              19981117
                                              US 1996-588771
                                                                 19960119
     US 5837224
                                              CA 1997-2241981 19970117
     CA 2241981
                        AA
                              19970724
     CA 2241981
                        С
                              20020319
     AU 9718317
                        A1
                              19970811
                                              AU 1997-18317
                                                                 19970117
     AU 701132
                        B2
                              19990121
                                              EP 1997-903847
     EP 883398
                        Α1
                              19981216
                                                                 19970117
             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             TE. FI
                                              CN 1997-191735
                                                                 19970117
     CN 1211178
                        Α
                              19990317
                              20020703
     CN 1086937
                        В
                              19990720
                                              BR 1997-7018
                                                                 19970117
     BR 9707018
                        Α
                                              JP 1997-526224
     JP 2000503660
                        T2
                              20000328
                                                                 19970117
                                              CZ 1998-2258
                                                                 19970117
     CZ 291530
                        В6
                              20030312
                                              NO 1998-3019
                                                                 19980629
     NO 9803019
                        Α
                              19980819
                                              LT 1998-91
                              19990625
                                                                 19980709
     LT 4515
                        В
                                              HK 1999-103976
                              20021122
                                                                 19990914
     HK 1018885
                        Α1
                                                            A 19960119
PRIORITY APPLN. INFO.:
                                           US 1996-588771
                                           WO 1997-US791
                                                             W 19970117
```

AB Photoaging of undamaged skin due to UVB irradiation exposure is inhibited by administering an agent that inhibits at least one of (1) the activity of UVB irradiation inducible MMPs in the skin, (2) one or both of the transcription factors AP-1 and NF-B or (3) at least one of the GTP binding proteins or kinases involved in the activation and/or production of jun of fos proteins that comprise AP-1; and topically administering said inhibitor to the skin prior to such exposure. A solution of 0.1% all-trans retinoic acid (I) in 70% ethanol and 30% propylene glycol was applied to the skin of volunteers for 48 h, the skin sites were then irradiated with 2 minimal erythema dose (1 MED = 30-50 mJ/cm2). I reduced UVB-induced MMP-1 and MMP-9 mRNAs, proteins and activity by 50-80%.

IT 142880-36-2, Galardin

RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses) (inhibition of skin photoaging by inhibitors of matrix

metalloproteinase production)

RN 142880-36-2 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L20 ANSWER 42 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1997:70379 HCAPLUS

DOCUMENT NUMBER:

126:171901

TITLE:

Preparation of peptide derivatives as inhibitors of

 $TNF-\alpha$ secretion

INVENTOR(S):

Black, Roy A.; Fitzner, Jeffrey N.; Sleath, Paul R.

Immunex Corporation, USA PATENT ASSIGNEE(S):

SOURCE:

U.S., 28 pp., Cont.-in-part of U.S. Ser. No. 110, 601,

abandoned.

CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5594106	А	19970114	US 1994-292547	19940818
US 5629285	A	19970513	US 1996-651363	19960522
PRIORITY APPLN.	INFO.:	US	1993-110601	19930823
		US	1994-292547	19940818

OTHER SOURCE(S):

MARPAT 126:171901

GΙ

II

Peptide derivs. having active groups capable of inhibiting $\mbox{TNF-}\alpha$ AB converting enzyme (TACE), such as hydroxamates, thiols, phosphoryls and carboxyls X(CHR1)mCHR2CONHCHR3CO(A)nNHBNH2 [I; X = hydroxamic acid, thiol, phosphoryl, carboxyl; m = 0-2; R1, R2, R3 = independently H, alkylene(cycloalkyl), OR4, NR4R5, halo, (un)substituted C1-8 alkyl, C1-8 alkylenearyl, aryl, (un)protected natural amino acid side chain, R6R7; R4, R5 = independently H, (un) substituted C1-8 alkyl; R6 = (un) substituted C1-8 alkyl; R7 = OR4, NR4R5, halo; n = 0-2; each A = same or different (un)protected α -amino acid radical; B = (un)substituted C2-8 alkylene], pharmaceutically acceptable salts thereof, and methods for preparing them are disclosed. I are useful in inhibiting TACE responsible for cleavage of TNF- α precursor to provide biol. active TNF- α . Thus, coupling of MeO2CCH2CH(CH2CHMe2)CO2Su (Su = succinimido; preparation qiven) with dipeptide H-Nal-Ala-NHCH2CH2NHZ (Nal = 2-naphthyl-L-alanine; Z = CO2CH2Ph; prepn given), condensation with hydroxylamine and catalytic hydrogenolysis, gave hydroxamate inhibitor II. II shows selective in vitro and in vivo inhibition of TNF- α secretion.

143457-42-5P 163847-77-6P 163958-63-2P

163958-73-4P 163958-74-5P 171235-71-5P

187034-27-1P 187034-28-2P 187034-29-3P

187034-30-6P 187034-31-7P 187034-32-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of peptide derivs. as inhibitors of TNF- α converting enzyme inhibitors)

RN 143457-42-5 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-3-(2-naphthalenyl)-L-alanyl-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 163847-77-6 HCAPLUS

CN L-Alaninamide, N-[(2R)-2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-3-(2-naphthalenyl)-L-alanyl-N-(2-aminoethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 163958-63-2 HCAPLUS

CN L-Alaninamide, N-[(2S)-2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-3-(2-naphthalenyl)-L-alanyl-N-(2-aminoethyl)- (9CI) (CA INDEX NAME)

RN 163958-73-4 HCAPLUS

CN L-Alaninamide, N-[(2R)-2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-3-(2-naphthalenyl)-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 163958-74-5 HCAPLUS

CN L-Alaninamide, N-[(2S)-2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-3-(2-naphthalenyl)-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 171235-71-5 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-3-(2-naphthalenyl)-L-alanyl-N-(2-aminoethyl)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H \\ N \\ O \\ HN \\ O \\ O \\ Me \\ \end{array}$$

RN 187034-27-1 HCAPLUS

CN L-Alaninamide, N2-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-L-arginyl-N-(2-aminoethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$H_2N$$
 H_2N
 H_2N
 H_2N
 H_3
 H_4
 H_5
 H_6
 H_6
 H_7
 H_8
 H_8

RN 187034-28-2 HCAPLUS

CN L-Alaninamide, N2-[(2R)-2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-L-lysyl-N-(2-aminoethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 187034-29-3 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-L-tyrosyl- (9CI) (CA INDEX NAME)

RN 187034-30-6 HCAPLUS

CN L-Serinamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-3-(2-naphthalenyl)-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 187034-31-7 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-3-methyl-L-valyl-N-(2-aminoethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 187034-32-8 HCAPLUS

CN L-Alaninamide, N2-[(2S)-2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-L-lysyl-N-(2-aminoethyl)- (9CI) (CA INDEX NAME)

IT 187034-36-2P 187034-41-9P 187034-44-2P 187034-47-5P 187034-49-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of peptide derivs. as inhibitors of TNF- α converting enzyme inhibitors)

RN 187034-36-2 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-3-(2-naphthalenyl)-L-alanyl-N-[2-[[(phenylmethoxy)carbonyl]amino]ethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 187034-41-9 HCAPLUS

CN L-Alaninamide, N5-[bis[[(phenylmethoxy)carbonyl]amino]methylene]-N2-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-L-ornithyl-N-[2-[(phenylmethoxy)carbonyl]amino]ethyl]- (9CI) (CA INDEX NAME)

RN 187034-44-2 HCAPLUS

CN L-Alaninamide, N2-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-N6-[(phenylmethoxy)carbonyl]-L-lysyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 187034-47-5 HCAPLUS

CN L-Alaninamide, N2-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-N6-(phenylmethyl)-L-lysyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 187034-49-7 HCAPLUS

CN L-Serinamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-3-(2-naphthalenyl)-L-alanyl-O-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

HCAPLUS COPYRIGHT 2004 ACS on STN L20 ANSWER 43 OF 63

ACCESSION NUMBER:

1997:51546 HCAPLUS

DOCUMENT NUMBER:

126:89699

TITLE:

Process for the preparation of activated glycomimetic

C-glycosides as selectin inhibitors Anderson, Mark Brian; Musser, John H.

INVENTOR(S):

Glycomed Incorporated, USA

PATENT ASSIGNEE(S): SOURCE:

PCT Int. Appl., 132 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 8

PATENT INFORMATION:

PA	PATENT NO.				ND :	DATE			A.	PPLI	CATIO	ON NC	ο.	DATE			
	-								-								
WO	9636	627		A:	1	1996	1121		W	0 19:	96-U	S6522	2	1996	0520		
	W:	ΑL,	AM,	ΑT,	AU,	AZ,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CZ,	DE,	DK,	EE,
		ES,	FI,	GB,	GE,	HU,	IS,	JP,	KΕ,	KG,	ΚP,	KR,	ΚZ,	LK,	LR,	LS,	LT,
		LU,	LV,	MD,	MG,	MK,	MN,	MW,	MX,	NO,	NZ,	PL,	PΤ,	RO,	RU,	SD,	SE,
		SG,	SI														
	RW: KE, LS				SD,	SZ,	UG,	ΑT,	ΒE,	CH,	DE,	DK,	ES,	FΙ,	FR,	GB,	GR,
	IE, II CA 2221589				MC,	ΝL,	PT,	SE,	BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	ML
. CA	2221	589		A	A	1996	1121		C.	A 19	96-22	2215	89	1996	0520		
AU	9658	552		A:	1	1996	1129		A	U 19	96-5	8552		1996	0520		
EP	8287	29		A.	1.	1998	0318		E	P 19	96-92	2015	8	1996	0520		
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	ΝL,	SE,	MC,	PT,
		ΙE,	FI														
JP	1150	7020		T	2	1999	0622		J	P 19	96-5	34893	3	1996	0520		
PRIORIT	Y APP	LN.	INFO	. :				1	US 1	995-	4461	85		1995	0519		
								1	WO 1	996-1	US65:	22		1996	0520		
OTHER S		(S):			MAR	PAT :	126:	8969	9								

GΙ

AB Combinatorial library and process for the preparation of title C-glycosides I (A = O, S, imino; Z = alkyl, alkenyl, arylalkyl; U = alkoxymethyl, carbonyl, R = H, Me, alkyl, sulfonyl, sugar; n = 1-3) as selectin inhibitors, are reported. Thus, 2-chloromethyl-3-(tetra-O-acetyl-α-L-mannopyranoside)-1-propene was prepared as selectin inhibitor (no data).

TT 185334-73-0P 185334-74-1P

185334-73-0P 185334-74-1P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(process for the preparation of activated glycomimetic C-glycosides as selectin inhibitors)

RN 185334-73-0 HCAPLUS

CN L-glycero-D-galacto-Nonitol, 2,6-anhydro-1,7,8,9-tetradeoxy-9[hydroxy[(3R)-3-[[[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2oxoethyl]amino]carbonyl]-5-methyl-1-oxohexyl]amino]-8-methylene- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

RN 185334-74-1 HCAPLUS

CN L-glycero-D-galacto-Nonitol, 2,6-anhydro-1,7,8,9-tetradeoxy-9-[[(2S)-2-[[(2R)-2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]amino]-3-(1H-indol-3-yl)-1-oxopropyl]amino]-8-methylene- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L20 ANSWER 44 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1996:452771 HCAPLUS

DOCUMENT NUMBER:

125:105111

TITLE:

Treatment of central nervous system inflammatory disease with matrix metalloprotease inhibitors

INVENTOR(S):

Gijbels, Koenraad; Steinman, Lawrence

PATENT ASSIGNEE(S):

The Board of Trustees of the Leland Stanford Junior

University, USA

SOURCE:

U.S., 10 pp. CODEN: USXXAM

DOCUMENT TYPE:

Patent English

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

KIND DATE APPLICATION NO. DATE PATENT NO. ----US 5532265 19960702 US 1994-348262 19941130 US 1994-348262 PRIORITY APPLN. INFO.: 19941130

A synthetic inhibitor of matrix metalloproteases, the tripeptide hydroxamate GM 6001, is administered to a patient suffering from an inflammatory disease of the central nervous system. The treatment diminishes the adverse effects of an inflammatory central nervous system disease associated with elevated matrix metalloprotease activity in the central nervous system. The effect is mediated primarily through restoration of the blood-CNS barrier.

142880-36-2, GM 6001

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(matrix metalloprotease inhibitor GM 6001 for treatment of adverse effects of central nervous system inflammatory disease associated with elevated matrix metalloprotease activity)

142880-36-2 HCAPLUS RN

Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-CN2-oxoethyl]-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L20 ANSWER 45 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1996:332351 HCAPLUS

DOCUMENT NUMBER:

125:11473

TITLE:

Preparation of N-(N-hydroxy-2-isobutyl-3-methylsuccinamyl) amino acid derivatives as collagenase

inhibitors

PATENT ASSIGNEE(S):

Fujisawa Pharmaceutical Co., Ltd., Japan

SOURCE:

Jpn. Kokai Tokkyo Koho, 72 pp.

CODEN: JKXXAF

DOCUMENT TYPE:

Patent

LANGUAGE:

Japanese

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.

KIND DATE

APPLICATION NO. DATE JP 08053403
PRIORITY APPLN. INFO.:

A2 19960227

JP 1995-151923 GB 1994-12350 19950619 19940620

OTHER SOURCE(S):

MARPAT 125:11473

GI

II

AB The title hydroxamic acid (I; R1 = H, OH-protective group; R2 = H, lower alkyl, NH2-protective group; R3 = H, 2-thienylthio; R4 = 2-pyridyl or its N-oxide, 4-pyridyl, Ph, 4-methoxyphenyl; R5 = HO, lower alkoxy, substituted NH2; provided that when R1 = R2 = H, R4 = 2-pyridyl or its N-oxide) or pharmaceutically acceptable salts, which are useful for the treatment or prevention of collagenase-mediated diseases such as destruction of joints in rheumatoid arthritis, pericementosis, ulcers of the cornea, tumor metastasis, deforming arthritis, osteoporosis, psoriasis, chronically active hepatitis, autoimmune keratitis, etc., are prepared Thus, N-succinyl-L-(2-pyridyl)alanine-N-methylamide derivative (R = HO) was condensed with hydroxylamine hydrochloride using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, N-hydroxybenzotriazole, and (Me2CH)2NEt in DMF at 0° for 1 h to give the title compound (II; R = HONH). This compound in vitro showed IC50 of 1.5 nM against human collagenase.

177162-56-0P 177162-59-3P 177162-62-8P 177162-67-3P 177162-72-0P 177162-73-1P 177162-74-2P 177162-75-3P 177162-76-4P 177162-77-5P 177162-78-6P 177162-79-7P 177162-83-3P 177162-84-4P 177162-91-3P 177162-92-4P 177163-05-2P 177163-07-4P 177163-18-7P 177163-19-8P 177163-21-2P 177163-51-8P 177163-52-9P 177163-53-0P 177163-75-6P 177163-77-8P 177163-78-9P 177163-78-9P 177164-06-6P

177164-07-7P 177164-08-8P 177164-09-9P 177164-16-8P 177164-17-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of N-(N-hydroxy-2-isobutyl-3-methyl-succinamyl)amino acid derivs. as collagenase inhibitors)

RN 177162-56-0 HCAPLUS

CN Butanediamide, N4-[2-[[2-(acetylamino)ethyl]amino]-2-oxo-1-(2-pyridinylmethyl)ethyl]-2-methyl-3-(2-methylpropyl)-N1-(phenylmethoxy)-, [2S-[2R*,3S*,4(R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 177162-59-3 HCAPLUS

CN Butanediamide, N4-[2-[[2-(acetylamino)ethyl]amino]-2-oxo-1-(2-pyridinylmethyl)ethyl]-N1-hydroxy-2-methyl-3-(2-methylpropyl)-,
[2S-[2R*,3S*,4(R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 177162-62-8 HCAPLUS

CN Propanoic acid, 2,2-dimethyl-, 2-(2,2-dimethyl-1-oxopropoxy)-4-methyl-5-(2-methylpropyl)-3,6,9,14-tetraoxo-8-(2-pyridinylmethyl)-2,7,10,13-tetraozapentadec-1-yl ester, [4S-(4R*,5S*,8R*)]- (9CI) (CA INDEX NAME)

RN 177162-67-3 HCAPLUS

CN Butanediamide, N4-[2-[[2-(acetylamino)ethyl]amino]-2-oxo-1-(2-pyridinylmethyl)ethyl]-N1-(2,2-dimethyl-1-oxopropoxy)-2-methyl-3-(2-methylpropyl)-, [2S-[2R*,3S*,4(R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 177162-72-0 HCAPLUS

CN Butanediamide, N4-[2-[[2-[[(dimethylamino)carbonyl]amino]ethyl]amino]-2oxo-1-(2-pyridinylmethyl)ethyl]-2-methyl-3-(2-methylpropyl)-N1(phenylmethoxy)-, [2S-[2R*,3S*,4(R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 177162-73-1 HCAPLUS

CN Butanediamide, 2-methyl-3-(2-methylpropyl)-N4-[2-[[2-[(4-

Searched by P. Ruppel

morpholinylcarbonyl)amino]ethyl]amino]-2-oxo-1-(2-pyridinylmethyl)ethyl]N1-(phenylmethoxy)-, [2S-[2R*,3S*,4(R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 177162-74-2 HCAPLUS

CN Butanediamide, 2-methyl-N4-[2-[[2-[methyl(4-morpholinylcarbonyl)amino]ethyl]amino]-2-oxo-1-(2-pyridinylmethyl)ethyl]-3-(2-methylpropyl)-N1-(phenylmethoxy)-, [2S-[2R*,3S*,4(R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 177162-75-3 HCAPLUS

CN Butanediamide, N4-[2-[[2-[[(hexahydro-1H-azepin-1-yl)carbonyl]amino]ethyl]amino]-2-oxo-1-(2-pyridinylmethyl)ethyl]-2-methyl-3-(2-methylpropyl)-N1-(phenylmethoxy)-, [2S-[2R*,3S*,4(R*)]]- (9CI) (CA INDEX NAME)

RN 177162-76-4 HCAPLUS

CN Butanediamide, 2-methyl-3-(2-methylpropyl)-N4-[2-oxo-1-(2-pyridinylmethyl)-2-[[2-[[[[4-(trifluoromethyl)phenyl]amino]carbonyl]amino]ethyl]amino]ethyl]-N1-(phenylmethoxy)-, [2S-[2R*,3S*,4(R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 177162-77-5 HCAPLUS

CN Butanediamide, N4-[2-[[2-[[(dimethylamino)carbonyl]amino]ethyl]amino]-2-oxo-1-(2-pyridinylmethyl)ethyl]-N1-hydroxy-2-methyl-3-(2-methylpropyl)-, [2S-[2R*,3S*,4(R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 177162-78-6 HCAPLUS

CN Butanediamide, N1-hydroxy-2-methyl-3-(2-methylpropyl)-N4-[2-[[2-[(4-

morpholinylcarbonyl)amino]ethyl]amino]-2-oxo-1-(2-pyridinylmethyl)ethyl]-,
[2S-[2R*,3S*,4(R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 177162-79-7 HCAPLUS

CN Butanediamide, N1-hydroxy-2-methyl-N4-[2-[[2-[methyl(4-morpholinylcarbonyl)amino]ethyl]amino]-2-oxo-1-(2-pyridinylmethyl)ethyl]-3-(2-methylpropyl)-, [2S-[2R*,3S*,4(R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 177162-80-0 HCAPLUS

CN Butanediamide, N4-[2-[[2-[[(hexahydro-1H-azepin-1-yl)carbonyl]amino]ethyl]amino]-2-oxo-1-(2-pyridinylmethyl)ethyl]-N1-hydroxy-2-methyl-3-(2-methylpropyl)-, [2S-[2R*,3S*,4(R*)]]- (9CI) (CA INDEX NAME)

RN 177162-81-1 HCAPLUS

CN Butanediamide, N1-hydroxy-2-methyl-3-(2-methylpropyl)-N4-[2-oxo-1-(2-pyridinylmethyl)-2-[[2-[[[[4-(trifluoromethyl)phenyl]amino]carbonyl]amino]ethyl]amino]ethyl]-, [2S-[2R*,3S*,4(R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 177162-82-2 HCAPLUS

CN Propanoic acid, 2,2-dimethyl-, 2-(2,2-dimethyl-1-oxopropoxy)-4,15-dimethyl-5-(2-methylpropyl)-3,6,9,14-tetraoxo-8-(2-pyridinylmethyl)-2,7,10,13,15-pentaazahexadec-1-yl ester, [4S-(4R*,5S*,8R*)]- (9CI) (CA INDEX NAME)

RN 177162-83-3 HCAPLUS

CN Propanoic acid, 2,2-dimethyl-, 2-(2,2-dimethyl-1-oxopropoxy)-4-methyl-5-(2-methylpropyl)-14-(4-morpholinyl)-3,6,9,14-tetraoxo-8-(2-pyridinylmethyl)-2,7,10,13-tetraazatetradec-1-yl ester, [4S-(4R*,5S*,8R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 177162-84-4 HCAPLUS

CN Butanediamide, N4-[2-[[2-[[(dimethylamino)carbonyl]amino]ethyl]amino]-2-oxo-1-(2-pyridinylmethyl)ethyl]-2-methyl-3-(2-methylpropyl)-N1-(1-oxopropoxy)-N1-[(1-oxopropoxy)methyl]-, [2S-[2R*,3S*,4(R*)]]- (9CI) (CAINDEX NAME)

Absolute stereochemistry.

RN 177162-90-2 HCAPLUS

CN Butanediamide, N4-[2-[[2-[[(dimethylamino)carbonyl]amino]ethyl]amino]-1[(4-methoxyphenyl)methyl]-2-oxoethyl]-2-methyl-3-(2-methylpropyl)-N1(phenylmethoxy)-, [2S-[2R*,3S*,4(R*)]]- (9CI) (CA INDEX NAME)

RN 177162-91-3 HCAPLUS

CN Butanediamide, N4-[2-[[2-[[(dimethylamino)carbonyl]amino]ethyl]amino]-1[(4-methoxyphenyl)methyl]-2-oxoethyl]-N1-hydroxy-2-methyl-3-(2methylpropyl)-, [2S-[2R*,3S*,4(R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 177162-92-4 HCAPLUS

CN Propanoic acid, 2,2-dimethyl-, 2-(2,2-dimethyl-1-oxopropoxy)-8-[(4-methoxyphenyl)methyl]-4,15-dimethyl-5-(2-methylpropyl)-3,6,9,14-tetraoxo-2,7,10,13,15-pentaazahexadec-1-yl ester, [4S-(4R*,5S*,8R*)]- (9CI) (CA INDEX NAME)

RN 177163-05-2 HCAPLUS

CN 2-Oxa-3,8,11,14-tetraazapentadecan-15-oic acid, 5-methyl-6-(2-methylpropyl)-4,7,10-trioxo-1-phenyl-9-(2-pyridinylmethyl)-, 2-methylpropyl ester, [5S-(5R*,6S*,9R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 177163-07-4 HCAPLUS

CN Butanediamide, N4-[2-[[2-[[(diethylamino)carbonyl]ethylamino]ethyl]amino]2-oxo-1-(2-pyridinylmethyl)ethyl]-2-methyl-3-(2-methylpropyl)-N1(phenylmethoxy)-, [2S-[2R*,3S*,4(R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 177163-18-7 HCAPLUS

CN 2-Oxa-3,8,11,14-tetraazapentadecan-15-oic acid, 5-methyl-6-(2-methylpropyl)-4,7,10-trioxo-1-phenyl-9-(2-pyridinylmethyl)-, phenyl ester, [5S-(5R*,6S*,9R*)]- (9CI) (CA INDEX NAME)

RN 177163-19-8 HCAPLUS

CN Butanediamide, N4-[2-[[2-[[(dimethylamino)carbonyl]methylamino]ethyl]amino]-2-oxo-1-(2-pyridinylmethyl)ethyl]-2-methyl-3-(2-methylpropyl)-N1-(phenylmethoxy)-, [2S-[2R*,3S*,4(R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 177163-21-2 HCAPLUS

CN Butanediamide, N4-[2-[[2-[[(diethylamino)carbonyl]methylamino]ethyl]amino]2-oxo-1-(2-pyridinylmethyl)ethyl]-2-methyl-3-(2-methylpropyl)-N1(phenylmethoxy)-, [2S-[2R*,3S*,4(R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 177163-22-3 HCAPLUS

CN Butanediamide, N4-[2-[[2-[[(dimethylamino)carbonyl]ethylamino]ethyl]amino]-2-oxo-1-(2-pyridinylmethyl)ethyl]-2-methyl-3-(2-methylpropyl)-N1-

(phenylmethoxy) -, [2S-[2R*,3S*,4(R*)]] - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 177163-30-3 HCAPLUS

CN Butanediamide, N4-[2-[[2-(acetylamino)ethyl]amino]-2-oxo-1-(4-pyridinylmethyl)ethyl]-2-methyl-3-(2-methylpropyl)-N1-(phenylmethoxy)-, [2S-[2R*,3S*,4(R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 177163-50-7 HCAPLUS

CN Butanediamide, 2-methyl-3-(2-methylpropyl)-N4-[2-oxo-2-[[2-[(2-pyridinylcarbonyl)amino]ethyl]amino]-1-(2-pyridinylmethyl)ethyl]-N1-(phenylmethoxy)-, [2S-[2R*,3S*,4(R*)]]- (9CI) (CA INDEX NAME)

RN 177163-51-8 HCAPLUS

CN Butanediamide, 2-methyl-3-(2-methylpropyl)-N4-[2-oxo-2-[[2-[(3-pyridinylcarbonyl)amino]ethyl]amino]-1-(2-pyridinylmethyl)ethyl]-N1-(phenylmethoxy)-, [2S-[2R*,3S*,4(R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 177163-52-9 HCAPLUS

CN Butanediamide, 2-methyl-3-(2-methylpropyl)-N4-[2-oxo-2-[[2-[(3-pyridinylcarbonyl)amino]ethyl]amino]-1-(4-pyridinylmethyl)ethyl]-N1-(phenylmethoxy)-, [2S-[2R*,3S*,4(R*)]]- (9CI) (CA INDEX NAME)

RN 177163-53-0 HCAPLUS

CN Butanediamide, 2-methyl-3-(2-methylpropyl)-N4-[2-oxo-2-[[2-[(2-pyridinylcarbonyl)amino]ethyl]amino]-1-(4-pyridinylmethyl)ethyl]-N1-(phenylmethoxy)-, [2S-[2R*,3S*,4(R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 177163-61-0 HCAPLUS

CN Carbamic acid, [2-[[2-[2-(hydroxyamino)-1-methyl-2-oxoethyl]-4-methyl-1-oxopentyl]amino]-1-oxo-3-(2-pyridinyl)propyl]amino]ethyl]-, 2-methylpropyl ester, [2R-[1(S*),2R*(S*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 177163-63-2 HCAPLUS

CN Butanediamide, N4-[2-[[2-[[(diethylamino)carbonyl]ethylamino]ethyl]amino]-2-oxo-1-(2-pyridinylmethyl)ethyl]-N1-hydroxy-2-methyl-3-(2-methylpropyl)-, [2S-[2R*,3S*,4(R*)]]- (9CI) (CA INDEX NAME)

RN 177163-74-5 HCAPLUS

CN Carbamic acid, [2-[[2-[2-(hydroxyamino)-1-methyl-2-oxoethyl]-4-methyl-1-oxopentyl]amino]-1-oxo-3-(2-pyridinyl)propyl]amino]ethyl]-, phenyl ester, [2R-[1(S*),2R*(S*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 177163-75-6 HCAPLUS

CN Butanediamide, N4-[2-[[2-[[(dimethylamino)carbonyl]methylamino]ethyl]amino]-2-oxo-1-(2-pyridinylmethyl)ethyl]-N1-hydroxy-2-methyl-3-(2-methylpropyl)-, [2S-[2R*,3S*,4(R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 177163-77-8 HCAPLUS

CN Butanediamide, N4-[2-[[2-[[(diethylamino)carbonyl]methylamino]ethyl]amino]-

2-oxo-1-(2-pyridinylmethyl)ethyl]-N1-hydroxy-2-methyl-3-(2-methylpropyl)-, [2S-[2R*,3S*,4(R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 177163-78-9 HCAPLUS

Butanediamide, N4-[2-[[2-[[(dimethylamino)carbonyl]ethylamino]ethyl]amino]-2-oxo-1-(2-pyridinylmethyl)ethyl]-N1-hydroxy-2-methyl-3-(2-methylpropyl)-, [2S-[2R*,3S*,4(R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 177163-86-9 HCAPLUS

CN Butanediamide, N4-[2-[[2-(acetylamino)ethyl]amino]-2-oxo-1-(4-pyridinylmethyl)ethyl]-N1-hydroxy-2-methyl-3-(2-methylpropyl)-, [2S-[2R*,3S*,4(R*)]]- (9CI) (CA INDEX NAME)

RN 177164-06-6 HCAPLUS

CN Butanediamide, N1-hydroxy-2-methyl-3-(2-methylpropyl)-N4-[2-oxo-2-[[2-[(2-pyridinylcarbonyl)amino]ethyl]amino]-1-(2-pyridinylmethyl)ethyl]-,
[2S-[2R*,3S*,4(R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 177164-07-7 HCAPLUS

CN Butanediamide, N1-hydroxy-2-methyl-3-(2-methylpropyl)-N4-[2-oxo-2-[[2-[(3-pyridinylcarbonyl)amino]ethyl]amino]-1-(2-pyridinylmethyl)ethyl]-, [2S-[2R*,3S*,4(R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 177164-08-8 HCAPLUS

CN Butanediamide, N1-hydroxy-2-methyl-3-(2-methylpropyl)-N4-[2-oxo-2-[[2-[(3-pyridinylcarbonyl)amino]ethyl]amino]-1-(4-pyridinylmethyl)ethyl]-,
[2S-[2R*,3S*,4(R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 177164-09-9 HCAPLUS

CN Butanediamide, N1-hydroxy-2-methyl-3-(2-methylpropyl)-N4-[2-oxo-2-[[2-[(2-pyridinylcarbonyl)amino]ethyl]amino]-1-(4-pyridinylmethyl)ethyl]-,
[2S-[2R*,3S*,4(R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 177164-16-8 HCAPLUS

CN 15-Oxa-2,5,8,13-tetraazaoctadecanoic acid, 13-(2,2-dimethyl-1-oxopropoxy)11,17,17-trimethyl-10-(2-methylpropyl)-6,9,12,16-tetraoxo-7-(2pyridinylmethyl)-, 2-methylpropyl ester, [7S-(7R*,10S*,11R*)]- (9CI) (CA
INDEX NAME)

177164-17-9 HCAPLUS RN

Propanoic acid, 2,2-dimethyl-, 2-(2,2-dimethyl-1-oxopropoxy)-13,15-diethyl-CN4-methyl-5-(2-methylpropyl)-3,6,9,14-tetraoxo-8-(2-pyridinylmethyl)-2,7,10,13,15-pentaazaheptadec-1-yl ester, [4S-(4R*,5S*,8R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L20 ANSWER 46 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

124:30411

ACCESSION NUMBER:

1995:978677 HCAPLUS

DOCUMENT NUMBER: TITLE:

Tryptophan derivatives as synthetic matrix

metalloprotease inhibitors and uses thereof

INVENTOR(S):

Levy, Daniel E.; Grobelny, Damian; Tang, Peng Cho; Holme, Kevin R.; Galardy, Richard E.; Schultz, Gregory

S.; Nematalla, Assad; Musser, John H.

PATENT ASSIGNEE(S):

Glycomed Incorp., USA

SOURCE:

PCT Int. Appl., 95 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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PATENT NO.
                      KIND DATE
                                          APPLICATION NO. DATE
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     WO 9519965
                            19950727
                      Α1
                                          WO 1995-US783
                                                           19950120
        W: AU, CA, JP
         RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
     US 5892112
                      Α
                            19990406
                                          US 1994-184727
                                                           19940121
     AU 9516049
                      Α1
                            19950808
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     EP 690841
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                                                           19950120
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE
     JP 09501183
                            19970204
                                                           19950120
                                          JP 1995-519668
                                        US 1994-184727 A 19940121
PRIORITY APPLN. INFO.:
                                       US 1990-616021
                                                        A1 19901120
                                       US 1990-615798 A2 19901121
                                       US 1991-747751 A1 19910820
                                       US 1991-747752 A2 19910820
                                       US 1992-817039 A2 19920107
                                       US 1992-881630 A1 19920512
                                       US 1993-44324
                                                        A2 19930407
                                       WO 1995-US783
                                                        W 19950120
OTHER SOURCE(S):
                        CASREACT 124:30411; MARPAT 124:30411
    Synthetic mammalian matrix metalloprotease inhibitors are disclosed, that
    are useful for treating or preventing diseases including skin disorders,
    keratoconus, restenosis, rheumatoid arthritis, wounds, cancer,
     angiogenesis and shock. The compds. include those of general formula
    R7ON(R6)CO(CHR1)nCH(R2)CON(R3)CH(R4)COX [where R1 = H, alkyl; R2 = H,
     alkyl, NHZ; Z = alkyl, alkanoyl, alkoxycarbonyl; or R1R2 = (CH2)3-5; R3 =
    H, alkyl; R4 = fused or conjugated (un) substituted bicycloarylmethylene; n
     = 0-2; X = OH, alkoxy, amino, alkylamino, amino acid or amide; R6 = H,
     alkyl; R7 = H, alkyl, acyl; amide group CONR3 may be replaced by selected
     isosteric groups]. For example, benzyl 4-methyl-2-oxopentanoate underwent
    Wittig reaction with Ph3P:CHCO2Me (100%), hydrogenation of the formed
    unsatd. diester (86%), peptide coupling of the obtained monoacid with
    H-Trp-NHMe.HCl and separation of diastereomers (83%), and reaction with NH2OH
     (56% and 72%), to give title compds. D,L- and L,L-HONHCOCH2CH(Bu-iso)CO-
    Trp-NHMe (I). In the phorbol ester-induced epidermal hyperplasia mouse
    model, D,L-I reduced ear thickness from 229% of control to only 140% of
    control. Over 40 synthetic examples are given, plus enzyme assays, and
    addnl. biol. tests showing activity against angiogenesis, chronic dermal
    wounds, peritonitis, metastasis, hypovolemic shock, and restenosis.
IT
    171347-98-1P 171348-01-9P 171348-02-0P
    171348-03-1P 171348-04-2P
    RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (intermediate; preparation of tryptophan derivs. as matrix metalloprotease
       inhibitors)
RN
    171347-98-1 HCAPLUS
CN
    Butanediamide, N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-[[3-(4-
    morpholinyl)propyl]amino]-2-oxoethyl]-2-(2-methylpropyl)-N4-
     (phenylmethoxy) -, (2R) - (9CI) (CA INDEX NAME)
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RN 171348-01-9 HCAPLUS

CN Butanediamide, N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-N4-(phenylmethoxy)-N4-(phenylmethyl)-, (2R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 171348-02-0 HCAPLUS

CN Butanediamide, N4-[(4-fluorophenyl)methoxy]-N4-[(4-fluorophenyl)methyl]-N1[1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-,
[S-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 171348-03-1 HCAPLUS

CN Propanoic acid, 2,2-dimethyl-, [[(3R)-3-[[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]amino]carbonyl]-5-methyl-1-oxohexyl](phenylmethoxy)amino]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 171348-04-2 HCAPLUS

CN Glycine, N-[(3R)-3-[[[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]amino]carbonyl]-5-methyl-1-oxohexyl]-N-(phenylmethoxy)-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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IT
     142880-36-2P 142880-37-3P 142880-40-8P
     142880-46-4P 142880-59-9P 142880-60-2P
     142880-62-4P 142902-71-4P 144007-87-4P
     159686-32-5P 159686-33-6P 159686-34-7P
     162550-05-2P 171347-79-8P 171347-80-1P
     171347-81-2P 171347-82-3P 171347-83-4P
     171347-84-5P 171347-85-6P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); USES (Uses)
        (preparation of tryptophan derivs. as matrix metalloprotease inhibitors)
RN
     142880-36-2 HCAPLUS
CN
     Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-
     2-oxoethyl]-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)
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RN 142880-37-3 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 142880-40-8 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-N1-methyl-2-(2-methylpropyl)- (9CI) (CA INDEX NAME)

RN 142880-46-4 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[2-[(2-hydroxyethyl)amino]-1-(1H-indol-3-ylmethyl)-2-oxoethyl]-2-(2-methylpropyl)- (9CI) (CA INDEX NAME)

RN 142880-59-9 HCAPLUS

CN Butanediamide, N1-[2-(dodecylamino)-1-(1H-indol-3-ylmethyl)-2-oxoethyl]-N4-hydroxy-2-(2-methylpropyl)-, monopotassium salt (9CI) (CA INDEX NAME)

● K

RN 142880-60-2 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[1-(1H-indol-3-ylmethyl)-2-oxo-2-[(1-phenylethyl)amino]ethyl]-2-(2-methylpropyl)- (9CI) (CA INDEX NAME)

RN 142880-62-4 HCAPLUS

CN Carbamic acid, [6-[[(2S)-2-[[(2S)-2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]amino]-3-(1H-indol-3-yl)-1-oxopropyl]amino]hexyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

RN 142902-71-4 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)- (9CI) (CA INDEX NAME)

RN 144007-87-4 HCAPLUS

CN Butanediamide, N4-(benzoyloxy)-N1-[1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)- (9CI) (CA INDEX NAME)

RN 159686-32-5 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[1-(1H-indol-3-ylmethyl)-2-oxo-2-(pentylamino)ethyl]-2-(2-methylpropyl)- (9CI) (CA INDEX NAME)

RN 159686-33-6 HCAPLUS

CN Butanediamide, N1-[2-(dodecylamino)-1-(1H-indol-3-ylmethyl)-2-oxoethyl]-N4-hydroxy-2-(2-methylpropyl)- (9CI) (CA INDEX NAME)

RN 159686-34-7 HCAPLUS

CN Butanediamide, N4-(acetyloxy)-N1-[1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & & & \\ H & & & & & \\ N & & & & \\ NH-C-CH-Bu-i \\ \\ CH_2-CH-C-NHMe \\ \\ O \\ \end{array}$$

RN 162550-05-2 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-[[3-(4-morpholinyl)propyl]amino]-2-oxoethyl]-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

RN 171347-79-8 HCAPLUS

CN Butanediamide, N1-hydroxy-N4-[1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-3-(2-methylpropyl)-2-(phenylmethyl)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & & & \\ & & & & & \\ & & & & \\ & & & \\ & & & \\ & \\ & & \\ & & \\ & \\ & & \\ & \\ & & \\$$

RN 171347-80-1 HCAPLUS

CN Butanediamide, N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-N4-(phenylmethoxy)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 171347-81-2 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-N4-(phenylmethyl)-, (2R)- (9CI) (CA INDEX NAME)

RN 171347-82-3 HCAPLUS

CN Butanediamide, N4-[(4-fluorophenyl)methyl]-N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 171347-83-4 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-N4-(methoxymethyl)-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 171347-84-5 HCAPLUS

CN Butanediamide, N4-(3,3-dimethyl-2-oxobutyl)-N4-hydroxy-N1-[1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-, [S-(R*,S*)]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

171347-85-6 HCAPLUS RN

Glycine, N-hydroxy-N-[(3R)-3-[[[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino) -2-oxoethyl]amino]carbonyl] -5-methyl-1-oxohexyl] - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

HCAPLUS COPYRIGHT 2004 ACS on STN L20 ANSWER 47 OF 63

ACCESSION NUMBER:

1995:934125 HCAPLUS

DOCUMENT NUMBER:

123:330041

TITLE:

Medical use of matrix metalloproteinase (MMP) inhibitors for inhibiting tissue contraction

Khaw, Peng Tee; Schultz, Gregory Scott

INVENTOR(S): PATENT ASSIGNEE(S):

Institute of Ophthalmology, UK; University of Florida

SOURCE:

PCT Int. Appl., 65 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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WO 9524921				A1 19950921					WO 1995-GB576					19950316					
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	RW:	KE,	MW,	SD,	SZ,	UG,	ΑT,	ΒE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	ΙE,	IT,		

LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

19950316 AU 9518985 19951003 AU 1995-18985 EP 750512 A1 19970102 EP 1995-911409 19950316 FR, GB, IT, NL R: CH, DE, 20000725 US 1996~716155 19961119 US 6093398 Α US 6379667 B1 20020430 US 1999-368307 19990803 A1 20021107 US 2002-135934 20020429 US 2002164319 GB 1994-5076 19940316 PRIORITY APPLN. INFO.: WO 1995-GB576 W 19950316 US 1996-716155 A3 19961119 US 1999-368307 A3 19990803

AB An MMP inhibitor, especially a collagenase inhibitor, is useful in the manufacture of

a medicament for the treatment of a natural or artificial tissue containing extracellular matrix components to inhibit contraction of the tissue, e.g. to prevent scar contracture in the skin or eye, by inhibiting invasion of the tissue by fibroblasts. This effect was demonstrated in collagen gels seeded with ocular fibroblasts and treated with the MMP inhibitor Galardin or with antibodies to MMP 1, 2, or 3.

IT 142880-36-2, Galardin

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(medical use of matrix metalloproteinase inhibitors for inhibiting tissue contraction)

RN 142880-36-2 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L20 ANSWER 48 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1995:750507 HCAPLUS

DOCUMENT NUMBER:

123:144644

TITLE:

Preparation of hydroxamic acid-containing amino acid and peptide derivatives as metalloproteinase and tumor

necrosis factor release inhibitors

INVENTOR(S):

Crimmin, Michael John; Ayscough, Andrew Paul; Beckett,

Raymond Paul

PATENT ASSIGNEE(S):

British Bio-Technology Ltd., UK

SOURCE:

PCT Int. Appl., 51 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND DATE	APPLICATION NO.	DATE				
WO 9424140	A1 19941027	WO 1994-GB808	19940418				
W: AU, CA,	CN, CZ, DE, FI,	GB, HU, JP, KR, NO, NZ	, PL, RU, US				
RW: AT, BE,	CH, DE, DK, ES,	FR, GB, GR, IE, IT, LU	, MC, NL, PT, SE				
AU 9465102	A1 19941108						
EP 694036	A1 · 19960131	EP 1994-912635	19940418				
EP 694036	B1 19970305						
R: BE, DE,	ES, FR, GB, IT,	NL, SE					
US 5696082	A 19971209	US 1996-530374	19960528				
PRIORITY APPLN. INFO	.:	GB 1993-7956	19930417				
		WO 1994-GB808	19940418				
OTHER SOURCE(S):	MARPAT 123:	144644					

Me
$$_{X}$$
 $_{O}$ $_{R}$ $_{N}$ $_{N}$

AB R1CHXCHR2CONHCHR3CONR4R5 [R1 = H alkyl, Ph, heterocyclyl, etc.; R2 = (phenyl)alkyl, heteroarylalkyl, etc.; R3 = ZCOR6, ZC6H4Z1R6, amino acid side chain, etc.; R4 = (CHR7CONH)mCOR6, H, alkyl, etc.; R5 = H, alkyl; R6 = pyranosylamino group Q1; R7 = H, amino acid side chain; X = CONHOH, CO2H; Z = alkylene; Z1 = CO,CH2CH2CO, OCH2CO, NHCH2CO] were prepared Thus, succinyltyrosine deriv, I (R = OH, X = CO2CMe2) was amidated by pyranosylamine Q2H and the product converted in 3 addnl. steps to I (R = Q2, X = NONHOH) which had IC50 of 20 and 600nM against collagenase and stromelysin, resp., in vitro.

IT 166811-02-5P 166811-03-6P 166811-05-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of hydroxamic acid-containing amino acid and peptide derivs. as metalloproteinase and tumor necrosis factor release inhibitors)

RN 166811-02-5 HCAPLUS

CN Glycinamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-L-phenylalanyl-N-[2-(acetylamino)-2-deoxy- β -D-glucopyranosyl]-, (R)-

(CA INDEX NAME)

Absolute stereochemistry.

RN166811-03-6 HCAPLUS

CNGlycinamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-Lphenylalanylglycyl-N-[2-(acetylamino)-2-deoxy-β-D-glucopyranosyl]-, (R) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN

166811-05-8 HCAPLUS Glycinamide, N-[2-[1-hydroxy-2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-CN $oxopentyl] - L - phenylalanyl - N - [2 - (acetylamino) - 2 - deoxy - \beta - D - deoxy - D - deoxy$ glucopyranosyl]-, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

IT 166811-10-5P 166811-11-6P 166811-17-2P 166811-24-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of hydroxamic acid-containing amino acid and peptide derivs. as metalloproteinase and tumor necrosis factor release inhibitors)

RN 166811-10-5 HCAPLUS

CN Glycinamide, N-[4-methyl-1-oxo-2-[2-oxo-2-[(phenylmethoxy)amino]ethyl]pent yl]-L-phenylalanyl-N-[3,4,6-tri-O-acetyl-2-(acetylamino)-2-deoxy- β -D-glucopyranosyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 166811-11-6 HCAPLUS

CN Glycinamide, N-[4-methyl-1-oxo-2-[2-oxo-2-[(phenylmethoxy)amino]ethyl]pent
yl]-L-phenylalanyl-N-[2-(acetylamino)-2-deoxy-β-D-glucopyranosyl]-,
(R)- (9CI) (CA INDEX NAME)

RN 166811-17-2 HCAPLUS

CN Glycinamide, N-[4-methyl-1-oxo-2-[2-oxo-2-[(phenylmethoxy)amino]ethyl]pent yl]-L-phenylalanylglycyl-N-[3,4,6-tri-O-acetyl-2-(acetylamino)-2-deoxy- β -D-glucopyranosyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 166811-24-1 HCAPLUS

CN Glycinamide, N-[2-[1-hydroxy-2-oxo-2-[(phenylmethoxy)amino]ethyl]-4-methyl-1-oxopentyl]-L-phenylalanyl-N-[3,4,6-tri-O-acetyl-2-(acetylamino)-2-deoxy- β -D-glucopyranosyl]-, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

HCAPLUS COPYRIGHT 2004 ACS on STN L20 ANSWER 49 OF 63

ACCESSION NUMBER:

1995:615213 HCAPLUS

DOCUMENT NUMBER:

123:33659

TITLE:

Preparation of peptides as inhibitors of tumor

necrosis factor-alpha (TNF-alpha) secretion

INVENTOR(S):

Black, Roy A.; Fitzner, Jeffrey N.; Sleath, Paul R.

PATENT ASSIGNEE(S): SOURCE:

Immunex Corp., USA PCT Int. Appl., 67 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English 2

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

	PATENT NO.			KIND DATE					APPLICATION NO. D										
	WO	9506031			A1 19950302					W	19:	94 - U	S934:	3	19940819				
		W:	AM,	ΑT,	ΑU,	BB,	ВG,	BR,	BY,	CA,	CH,	CN,	CZ,	DE,	DK,	ES,	FΙ,	GB,	
			GE,	HU,	JP,	KE,	KG,	KΡ,	KR,	KΖ,	LK,	LT,	LU,	LV,	MD,	MG,	MN,	MW,	
			NL,	NO,	NZ,	PL,	PT,	RO,	RU,	SD,	SE,	SI,	SK,	ТJ,	TT,	UA,	UZ,	VN	
		RW:	KE,	MW,	SD,	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	
			NL,	PT,	SE,	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	ΜL,	MR,	NE,	SN,	TD,	TG
	ΑU	9475	694		A.	1	1995	0321	AU 1994-75694						1994	0819			
	ΑU	687436			B2 19980226														
	ΕP	7156	19		A:	1 .	1996	0612		E	199	94 - 9:	2594	0	1994	0819			
		R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	ΙE,	IT,	LI,	LU,	MC,	NL,	PT,	SE
	JΡ	0950	3201		T	2	1997	0331		J)	2 19	94-5	0766	В	1994	0819			
	FI	9600	803		Α		1996	0422		\mathbf{F}	[19	96-8	03		1996	0222			
	NO	9600	723		Α		1996	0223		N	199	96-72	23		1996	0223			
	ΑU	9850	302		A:	1	1998	0305		ΑŪ	J 19	98-5	0302		1998	0106			
PRIO	PRIORITY APPLN. INFO.:								1	US 19	993-1	1106	01		1993	0823			
									1	US 19	994-	1830	19		1994	0118			
									1	WO 19	994-T	JS934	43		1994	0819			,
OTHER SOURCE(S): M							MARPAT 123:33659												

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X[CHR1]mCHR2CONHCHR3CO[A]nNH-B-NH2 [X = hydroxamic acid, thiol, phosphoryl, CO2H; m = 0,1,2; R1 - R3 = H, alkylene-cycloalkyl, OR4, SR4, NR4R5, halo, (un) substituted C1-8 alkyl, C1-8 alkylene-aryl, aryl, (un)protected side chain of a naturally occurring α -amino acid, or group R6R7; wherein R6 = (un) substituted C1-8 alkyl and R7 = OR4, SR4, NR4R5, or halo; wherein R4, R5 = H, (un) substituted $C\dot{1}$ -8 alkyl; n = 0,1,2; provided that when n = 1, A = (un) protected amino acid radical; when n = 12, A = same or different (un)protected amino acid radical; B = (un) substituted C2-8 alkylene] and pharmaceutically acceptable salts thereof, which are inhibitors of metalloproteases and, in particular, $\mathtt{TNF-}\alpha$ converting enzyme (TACE), are prepared. These peptides have active groups capable of inhibiting TACE responsible for cleavage of TNF- α precursor to provide biol. active TNF- α and are useful for treating a mammal having a disease characterized by an overprodn. or an unregulated production of TNF- α . Thus, DL-2-isobutyl-3-(methoxycarbonyl)propionic acid N-hydroxysuccinimide ester (preparation given) was added to a solution of L-3-(2-naphthyl)alanyl-L-alanine 2-(benzyloxycarbonylamino)ethylamide and Et3N in DMF and stirred at room temperature for 18 h to give a dipeptide derivative (I; R = MeO, A1 = CO2CH2Ph) (89%

yield), which was condensed with HONH2 in MeOH containing KOH in an ice-bath to give 86% I (R = HONH, A1 = CO2CH2Ph). The latter compound was hydrogenolyzed over 10% Pd-C in glacial AcOH to give a title peptide I.AcOH (R = HONH, A1 = H). The latter peptide at 200 μM in vitro inhibited TNF- α release from T-cells by 72 and 63% at 24 and 48 h, resp., while there was no inhibitory effect on the release of TNF- β or interferon- γ .

IT 163847-98-1P 163848-00-8P 163848-03-1P 163848-05-3P 163848-20-2P 163958-73-4P 163958-74-5P 163958-76-7P 163958-78-9P 163958-80-3P 163958-82-5P 163958-85-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate for preparation of peptides as inhibitors of TNF- α converting enzyme and TNF- α secretion)

RN 163847-98-1 HCAPLUS

CN L-Alaninamide, N5-[bis[[(phenylmethoxy)carbonyl]amino]methylene]-N2-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-L-ornithyl-N-[2-[(phenylmethoxy)carbonyl]amino]ethyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

RN 163848-00-8 HCAPLUS

CN L-Alaninamide, N2-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-N6-[(phenylmethoxy)carbonyl]-L-lysyl-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 163848-03-1 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-O-(phenylmethyl)-L-tyrosyl-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 163848-05-3 HCAPLUS

CN L-Serinamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-3-(2-naphthalenyl)-L-alanyl-0-(phenylmethyl)-, (R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 163848-20-2 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-3-(2-naphthalenyl)-L-alanyl-N-[2-[[(phenylmethoxy)carbonyl]amino]ethyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 163958-73-4 HCAPLUS

CN L-Alaninamide, N-[(2R)-2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-3-(2-naphthalenyl)-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 163958-74-5 HCAPLUS

CN L-Alaninamide, N-[(2S)-2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-3-(2-naphthalenyl)-L-alanyl- (9CI) (CA INDEX NAME)

RN 163958-76-7 HCAPLUS

CN L-Alaninamide, N5-[bis[[(phenylmethoxy)carbonyl]amino]methylene]-N2-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-L-ornithyl-N-[2-[(phenylmethoxy)carbonyl]amino]ethyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

RN 163958-78-9 HCAPLUS

CN L-Alaninamide, N2-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-N6-[(phenylmethoxy)carbonyl]-L-lysyl-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 163958-80-3 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-0-

(phenylmethyl)-L-tyrosyl-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 163958-82-5 HCAPLUS

CN L-Serinamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-3-(2-naphthalenyl)-L-alanyl-O-(phenylmethyl)-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 163958-85-8 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-3-(2-naphthalenyl)-L-alanyl-N-[2-[[(phenylmethoxy)carbonyl]amino]ethyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT 163847-78-7P 163847-82-3P 163847-83-4P 163847-84-5P 163847-87-8P 163847-88-9P 163958-64-3P 163958-65-4P 163958-66-5P

163958-67-6P 163958-68-7P 163958-69-8P 163958-70-1P 163958-71-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of peptides as inhibitors of TNF- α converting enzyme and TNF- α secretion)

RN 163847-78-7 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-3-(2-naphthalenyl)-L-alanyl-N-(2-aminoethyl)-, (R)-, monoacetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 163847-77-6 CMF C26 H37 N5 O5

Absolute stereochemistry.

CM 2

CRN 64-19-7 CMF C2 H4 O2

RN 163847-82-3 HCAPLUS

CN L-Alaninamide, N2-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-L-arginyl-N-(2-aminoethyl)-, dihydrochloride, (R)- (9CI) (CA INDEX NAME)

●2 HCl

RN 163847-83-4 HCAPLUS

CN L-Alaninamide, N2-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-L-lysyl-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 163847-84-5 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-L-tyrosyl-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 163847-87-8 HCAPLUS

CN L-Serinamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-3-(2-naphthalenyl)-L-alanyl-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 163847-88-9 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-4-methyl-L-leucyl-N-(2-aminoethyl)-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$\begin{array}{c|c} CMe_3 \\ H \\ N \\ S \\ N \\ O \\ I-Bu \\ R \\ O \\ O \\ H \end{array} OH$$

RN 163958-64-3 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-3-(2-naphthalenyl)-L-alanyl-N-(2-aminoethyl)-, (S)-, monoacetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 163958-63-2 CMF C26 H37 N5 O5

CM 2

CRN 64-19-7 CMF C2 H4 O2

RN 163958-65-4 HCAPLUS

CN L-Alaninamide, N2-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-L-arginyl-N-(2-aminoethyl)-, dihydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$H_2N$$
 H_2N
 H_2N
 H_3
 H_4
 H_2N
 H_4
 H_5
 H_6
 H_7
 H_8
 H_8

●2 HC1

RN 163958-66-5 HCAPLUS

CN L-Alaninamide, N2-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-L-lysyl-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 163958-67-6 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-L-tyrosyl-, (S)- (9CI) (CA INDEX NAME)

RN 163958-68-7 HCAPLUS

CN L-Serinamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-3-(2-naphthalenyl)-L-alanyl-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 163958-69-8 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-3-(2-naphthalenyl)-L-alanyl-N-methyl-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 163958-70-1 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-3-(2-naphthalenyl)-L-alanyl-N-methyl-, (S)- (9CI) (CA INDEX NAME)

RN 163958-71-2 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-4-methyl-L-leucyl-N-(2-aminoethyl)-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L20 ANSWER 50 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1995:248590 HCAPLUS

DOCUMENT NUMBER:

122:23869

TITLE:

Preparation of synthetic matrix metalloprotease

inhibitors as pharmaceuticals.

INVENTOR(S):

Galardy, Richard Edward; Grobelny, Damian; Schultz,

Gregory Scott

PATENT ASSIGNEE(S):

Glycomed Incorp, USA

SOURCE:

PCT Int. Appl., 60 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

7

PATENT INFORMATION:

PA	TENT NO.	KIN	D DATE	A	PPLICATIO	N NO.	DATE		
WO		A1 CA, JP,	19941013 NO	We	1994-US	3600	19940401		
	RW: AT,	BE, CH,	DE, DK, ES,	FR, GB,	GR, IE,	IT, LU,	MC, NL,	PT,	SE
CA	2160139	AA	19941013	C	1994-21	60139	19940401		
AU	9465542	A1	19941024	A	J 1994-65	542	19940401		
EP	692931	A 1	19960124	E	9 1994-91	3345	19940401		
	R: AT,	BE, CH,	DE, DK, ES,	FR, GB,	GR, IE,	IT, LI,	LU, MC,	NL,	PT, SE
JР	08511509	. T2	19961203	J	9 1994-52	2412	19940401		
AU	9883118	A1	19990128	A'	J 1998-83	118	19980904		
PRIORIT	Y APPLN.	INFO.:		US 1	993-44324	А	19930407		
				AU 1	994-65542	A3	19940401		

WO 1994-US3600 W 19940401

OTHER SOURCE(S):

MARPAT 122:23869

AB Skin disorders, keratoconus, restenosis, wounds, and diseases that involve uncontrolled angiogenesis, are treated with synthetic mammalian matrix metalloprotease inhibitors. The inhibitors are R70NR6CO(CHR1)nCHR2CONR3CHR4COX or R70NR6CO(CHR1)mCR1:CR2CONR3CHR4COX [R1,R2,R3=H, alkyl;R1R2=(CH2)p;R4=fused or conjugated bicycloaryl methylene;X=OR5,NHR5;R5=H, alkyl, amino acid residue, etc.;R6=H, alkyl;R7=R6,acyl;m=0,1;n=0,1,2;p=3,4,5;the CONR3-amide bond is optionally replaced by CHNR3,CH2CHR3, etc.]. N-[D,L-2-isobutyl-3-(N'-hydroxycarbonylamido)propanoyl]tryptophan methylamide (preparation given) inhibited angiogenesis in the rat eye with induced Walker 256 carcinoma.

IT 142880-36-2P 142880-37-3P 142880-40-8P 142880-46-4P 142880-60-2P 142880-62-4P

142902-71-4P 144007-87-4P 159686-32-5P

159686-33-6P 159686-34-7P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of synthetic matrix metalloprotease inhibitors as pharmaceuticals)

RN 142880-36-2 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 142880-37-3 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 142880-40-8 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-

oxoethyl]-N1-methyl-2-(2-methylpropyl)- (9CI) (CA INDEX NAME)

RN 142880-46-4 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[2-[(2-hydroxyethyl)amino]-1-(1H-indol-3-ylmethyl)-2-oxoethyl]-2-(2-methylpropyl)- (9CI) (CA INDEX NAME)

RN 142880-60-2 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[1-(1H-indol-3-ylmethyl)-2-oxo-2-[(1-phenylethyl)amino]ethyl]-2-(2-methylpropyl)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & CH_2-C-NH-OH \\ \hline & NH-C-CH-Bu-i \\ \hline & CH_2-CH-C-NH-CH-Me \\ \hline & O & Ph \\ \end{array}$$

RN 142880-62-4 HCAPLUS

CN Carbamic acid, [6-[[(2S)-2-[[(2S)-2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]amino]-3-(1H-indol-3-yl)-1-oxopropyl]amino]hexyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

RN 142902-71-4 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)- (9CI) (CA INDEX NAME)

RN 144007-87-4 HCAPLUS

CN Butanediamide, N4-(benzoyloxy)-N1-[1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)- (9CI) (CA INDEX NAME)

RN 159686-32-5 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[1-(1H-indol-3-ylmethyl)-2-oxo-2-(pentylamino)ethyl]-2-(2-methylpropyl)- (9CI) (CA INDEX NAME)

RN 159686-33-6 HCAPLUS

CN Butanediamide, N1-[2-(dodecylamino)-1-(1H-indol-3-ylmethyl)-2-oxoethyl]-N4hydroxy-2-(2-methylpropyl)- (9CI) (CA INDEX NAME)

RN 159686-34-7 HCAPLUS

CN Butanediamide, N4-(acetyloxy)-N1-[1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)- (9CI) (CA INDEX NAME)

L20 ANSWER 51 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1995:19442 HCAPLUS

DOCUMENT NUMBER:

122:230797

TITLE:

Inhibition of tumor necrosis factor (TNF) production

INVENTOR(S):

Crimmin, Michael John; Galloway, William Alan;

Gearing, Andrew John Hubert

PATENT ASSIGNEE(S):

British Bio-Technology Ltd., UK

SOURCE:

PCT Int. Appl., 50 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

: 1

PATENT INFORMATION:

PATENT NO.

KIND DATE

APPLICATION NO. DATE

WO 9410990 A1 19940526 WO 1993-GB2331 19931112 W: AU, CA, DE, ES, FI, GB, JP, KR, NO, NZ, US RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE AU 9454301 Α1 19940608 AU 1994-54301 19931112 EP 1993-924754 EP 667770 A1 19950823 19931112 EP 667770 В1 19970319 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE JP 1993-511862 JP 08505605 T2 19960618 19931112 AT 1993-924754 AT 150300 19970415 19931112 Т3 19970701 ES 1993-924754 ES 2101358 19931112 US 5691382 Α 19971125 US 1995-436190 19950512 GB 1992-23904 PRIORITY APPLN. INFO.: 19921113 WO 1993-GB2331 19931112

Certain hydroxamic acid derivs., previously known as inhibitors of matrix AΒ metalloproteinases (e.g. collagenase) are capable of inhibiting the production of TNF by cells, and thus are useful in the management of diseases or conditions mediated by overprodn. of, or over-responsiveness to, TNF. compds. in question are known in the art from the following patent publications: US 4599361, EP-A-0236872, EP-A-0274453, WO 90/05716, WO 90/05719,WO 91/02716, EP-A-0489577, EP-A-0489579, EP-A-0497192, WO 92/13831, WO 92/22523, WO 93/09090, and WO 93/09097. They have general formula CH(R1)(CONHOH)CH(R2)C(O)NHCH(R3)C(O)N(R4)(R5) or CH(R1)[N(OH)(CO)H]CH(R2)C(O)NHCH(R3)C(O)N(R4)(R5), in which substituents R1-R5 may vary widely according to the disclosures of those patent publications. Prevention of e.g. TNF release from phorbol myristate acetate-stimulated human monocytic cell line U937 by compds. of the invention is described.

IT 155865-40-0

RL: BIOL (Biological study)

(TNF production inhibition by)

155865-40-0 HCAPLUS RN

Butanediamide, N1-[2-[(2-aminoethyl)amino]-2-oxo-1-(phenylmethyl)ethyl]-N4-CN hydroxy-2-(2-methylpropyl)-, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$H_2N$$
 N
 H
 S
 N
 Ph
 $i-Bu$
 R
 O
 O
 N
 H
 OH

L20 ANSWER 52 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1994:426909 HCAPLUS

DOCUMENT NUMBER:

121:26909

TITLE:

Vasoactive peptide inhibition

INVENTOR (S):

Crimmin, Michael John; Bone, Elisabeth Ann; Wood, Lars

Michael

PATENT ASSIGNEE(S):

British Bio-Technology Ltd., UK

SOURCE:

PCT Int. Appl., 15 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

KIND DATE APPLICATION NO. DATE PATENT NO. -----______ A2 19940414 WO 1993-GB2044 19931001 WO 9407527 A3 19940721 WO 9407527

W: AU, CA, FI, GB, JP, KR, NO, NZ, PT, US

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

AU 1993-48316 AU 9348316 A1 19940426 19931001

GB 1992-20845 PRIORITY APPLN. INFO .: 19921003 WO 1993-GB2044

Certain known hydroxamic acid derivs. and their salts are useful as AB inhibitors of the conversion of big endothelin (I) to endothelin by a putative endothelin converting enzyme, and are useful in the management of diseases mediated by overprodn. of, over-responsiveness to, endothelin in mammals, e.g. hypertension. Thus, i.v. administration of 1mg [4-(N-hydroxyamino)-2R-isobutylsuccinyl]-L-phenylalanine/kg in rats 5 min before i.v. administration of I inhibited its activity by 62%.

IT 155832-42-1 155865-40-0

RL: BIOL (Biological study)

(as inhibitor of big endothelin conversion to endothelin)

155832-42-1 HCAPLUS RN

L-Phenylalaninamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-CNoxopentyl]-L-phenylalanyl-N-methyl-, (R)- (9CI) (CA INDEX NAME)

155865-40-0 HCAPLUS RN

Butanediamide, N1-[2-[(2-aminoethyl)amino]-2-oxo-1-(phenylmethyl)ethyl]-N4-CNhydroxy-2-(2-methylpropyl)-, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

HCAPLUS COPYRIGHT 2004 ACS on STN L20 ANSWER 53 OF 63

1994:245779 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 120:245779

Inhibition of angiogenesis by synthetic matrix TITLE:

Galardy, Richard E.

metalloprotease inhibitors

INVENTOR(S):

PATENT ASSIGNEE(S): Glycomed, Inc., USA

PCT Int. Appl., 51 pp. SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE:

English

7

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT 1	O. KIND	DATE	AI	PPLICATIO	NO.	DATE			
	741 A2 741 A3		WC	1993-US	554	19930104			
W :	AU, CA, DK, J AT, BE, CH, D	P, NO	FR GB	GR IE	וו.ז ידד	MC NT.	DΨ	SE.	
US 52683	384 A	19931207	US	1992-81	7039	19920107	•		
AU 93343	332 A1	19930803	JA	J 1993-34	1332	19930104			
JP 07503	3007 T2	19950330	JI	1993-51	2526	19930104	-		
EP 66382	23 A1	19950726	EI	1993-90	2938	19930104			
EP 66382	23 B1	20001122						,	
R:	AT, BE, CH, D	E, DK, ES,	FR, GB,	GR, IE,	IT, LI	, LU, MC,	NL,	PT,	SE
AT 19766	57 E	20001215	A7	1993-90	2938	19930104			
PRIORITY APPI	N. INFO.:		US 19	992-81703	9 A	19920107			
			US 19	990-61579	98 A2	19901121			
			US 19	991-74775	51 A2	19910820			
			US 19	991-74775	52 A2	19910820			
			WO 19	993-US54	Α	19930104			

OTHER SOURCE(S):

MARPAT 120:245779

Peptides R7ONR6CO[CHR1]nCHR2CONR3CHR4COR5 [R1 = H, alkyl; R2 = alkyl; R1R2 = alkylene; R3 = H, alkyl; R4 = fused or conjugated (un)substituted bicycloarylmethyl; R5 = (un)substituted OH, NH2, amino acid residue; R6 = H, alkyl; R7 = H, alkyl, acyl; n = 0-2] were prepared as angiogenesis and metalloproteinase inhibitors. Thus, HONHCOCH2CH(CH2CHMe2)CO-L-Trp-NHMe (I) was prepared as a mixture of diastereomers from Me2CHCH2COCO2Na via reaction with Ph3P:CHCO2Me and H-Trp-NHMe.HCl. The isomers had matrix metalloproteinase-inhibiting Ki of 10 and 150 nM, resp.

IT 143985-51-7P

RL: SPN (Synthetic preparation); PREP (Preparation) (intermediate in preparation of metalloproteinase inhibiting hydroxylaminocarbonylalkanoyltryptophanamides)

RN 143985-51-7 HCAPLUS

CN Butanediamide, N1-[2-(dodecylamino)-1-(1H-indol-3-ylmethyl)-2-oxoethyl]-N4-hydroxy-2-(2-methylpropyl)-, monopotassium salt, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

K

142880-53-3P 142880-58-8P 142880-62-4P 143985-20-0P 143985-22-2P 144069-98-7P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation and metalloproteinase inhibiting activity of)

RN 142880-36-2 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethy1)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropy1)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 142880-37-3 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 142880-38-4 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1R)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

RN 142880-53-3 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[1-(1H-indol-3-ylmethyl)-2-oxo-2-(pentylamino)ethyl]-2-(2-methylpropyl)-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 142880-58-8 HCAPLUS

CN Butanediamide, N1-[2-(dodecylamino)-1-(1H-indol-3-ylmethyl)-2-oxoethyl]-N4-hydroxy-2-(2-methylpropyl)-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 142880-62-4 HCAPLUS

CN Carbamic acid, [6-[[(2S)-2-[[(2S)-2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]amino]-3-(1H-indol-3-yl)-1-oxopropyl]amino]hexyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

RN 143985-20-0 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-N1-methyl-2-(2-methylpropyl)-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 143985-22-2 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[2-[(2-hydroxyethyl)amino]-1-(1H-indol-3-ylmethyl)-2-oxoethyl]-2-(2-methylpropyl)-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 144069-98-7 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[1-(1H-indol-3-ylmethyl)-2-oxo-2-[(1-phenylethyl)amino]ethyl]-2-(2-methylpropyl)-, [2S-[N1[R*(R*)],2R*]]- (9CI) (CA INDEX NAME)

IT 142880-53-3P 142880-75-9P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)

RN 142880-53-3 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[1-(1H-indol-3-ylmethyl)-2-oxo-2-(pentylamino)ethyl]-2-(2-methylpropyl)-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 142880-75-9 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1R)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L20 ANSWER 54 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1994:217274 HCAPLUS

DOCUMENT NUMBER: TITLE:

120:217274 Succinamide derivative matrix-metalloprotease

inhibitors

INVENTOR (S):

Singh, Jasbir; Morgan, Barry A.; Gainor, James A.;

Gordon, Thomas D.; Wahl, Robert C.

PATENT ASSIGNEE(S):

Sterling Winthrop, Inc., USA

SOURCE:

U.S., 7 pp. CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

APPLICATION NO. DATE

PATENT NO.

KIND DATE

Ι

US 5256657
PRIORITY APPLN. INFO.:
OTHER SOURCE(S):

A 19931026

US 1991-747887 US 1991-747887 19910819 19910819

MARPAT 120:217274

GΙ

$$\begin{array}{c|c} O & CH_2R^1 & O \\ \hline & H & \\ N & \\ N & \\ O & CH_2R^2 \end{array} (CH_2)_{\mathfrak{m}}SO_n (CH_2)_{p}NR^3R^4$$

The title compds., i.e. succinimide derivs. I (X = HO, HONH; R1 = alkyl; R2 = alkyl, amino acid side chain derivative etc.; R3 = alkyl; R4 = H, alkyl, etc.; m = 2-6; n = 0-1; p = 2-6) are claimed. I are agents for the treatment of diseases in which matrix metallo protease-promoted connective tissue remodeling is a causative factor (for example rheumatoid arthritis or cancer). I inhibited human fibroblast collagenase (collagenase inhibitors). An example compound, N-[[[[[(aminoethyl)thio]ethyl]amino]carbo nyl] (indolyl)ethyl]succinamide II was prepared in several steps. The in vitro IC50 of II toward human fibroblast collagenase was 8.8 μM.

II

IT 153465-42-0P 153465-46-4P

RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of, as collagenase inhibitor)

RN 153465-42-0 HCAPLUS

CN Butanediamide, N1-[2-[[2-[[2-(dimethylamino)ethyl]thio]ethyl]amino]-1-(1H-indol-3-ylmethyl)-2-oxoethyl]-N4-hydroxy-2-(2-methylpropyl)-, [S-(R*,S*)]-(9CI) (CA INDEX NAME)

153465-46-4 HCAPLUS RN

Butanediamide, N4-hydroxy-N1-[1-(1H-indol-3-ylmethyl)-2-[[2-[[2-(4-CNmorpholinyl)ethyl]thio]ethyl]amino]-2-oxoethyl]-2-(2-methylpropyl)-, [S-(R*,S*)]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

L20 ANSWER 55 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1993:473118 HCAPLUS

DOCUMENT NUMBER:

119:73118

TITLE:

Peptide derivatives of collagenase inhibitor

INVENTOR(S):

Gray, Robert D.; Spatola, Arno F.; Darlan, Krzysztof

PATENT ASSIGNEE(S):

Research Corp. Technologies, Inc., USA

SOURCE:

PCT Int. Appl., 87 pp. CODEN: PIXXD2

Patent

DOCUMENT TYPE: LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9222523	A2	19921223	WO 1992-US5118	19920612
WO 9222523	A3	19930121		
W: AU, CA,	JP, KR			
RW: AT, BE,	CH, DE	, DK, ES, FR,	GB, GR, IT, LU, MC	, NL, SE
AU 9222282	A1	19930112	AU 1992-22282	19920612
US 5387610	Α	19950207	US 1992-981149	19921124
US 5616605	Α	19970401	US 1994-287320	19940808
PRIORITY APPLN. INFO	.:		US 1991-715948	19910614
			WO 1992-US5118	19920612
			US 1992-981149	19921124
OTHER SOURCE(S):	MA	RPAT 119:7311	8	

GI

Peptide derivs. R7ONHCOCHRCHR1CONHCR2R9-B-X-D [R and R1 = H, alkyl, aryl, AΒ aralkyl; R2 = (un)substituted aralkyl or heterocyclic alkyl; B = CONR6, R6NCO, CH2SO, CH2SO2, CH2NH, COCH2, CH:CH, C(OH)CH2NH2, CO-AA1 (AA1 =

amino acid residue), X = bond, alkylene, (CR5R10)mCONR8, (CR5R10)mCH2O, (CR5R10)mCO2; R9 and R10 = H, Me or Et; D, R5, R6, R7, and R8 = H or alkyl; m = 1, 2, 3] were prepared as collagenase inhibitors. Thus, Me2CHCH2CH(CO2H)CH2CO2CMe3 was coupled with H-L-Nal-L-Ala-NH2.HCl (Nal = naphthylalanine) by EtN:C:N(CH2)3NMe2 (EDC) in the presence of Et3N in DMF to give the corresponding condensed product, which was sequentially de-tert-butylated by HCl/dioxane, condensed with H2NOCH2Ph by EDC and debenzylated by hydrogenolysis to give peptide derivative I as a mixture of 2 diastereoisomers. The peptide derivs. were assayed for enzyme-inhibiting activity using pig synovial collagenase, pig synovial gelatinase, and recombinant human fibroblast collagenase.

IT 148745-35-1 148745-36-2 148745-37-3
148745-38-4 148811-73-8 148811-74-9
148811-75-0 148811-76-1 148811-77-2
148811-78-3 148811-79-4 148811-80-7
148811-81-8 148811-82-9 148811-83-0
148811-84-1 148811-85-2 148811-86-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(collagenase-inhibiting activity of)

RN 148745-35-1 HCAPLUS
CN L-Alaninamide, 4-chloro-N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-L-phenylalanyl-, (R)- (9CI) (CA INDEX NAME)

RN 148745-36-2 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-3-methoxy-0-methyl-L-tyrosyl-, (R)- (9CI) (CA INDEX NAME)

RN 148745-37-3 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-3-(1-naphthalenyl)-L-alanyl-N-methyl-, (R)- (9CI) (CA INDEX NAME)

RN 148745-38-4 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxymethylamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-L-phenylalanyl-, (R)- (9CI) (CA INDEX NAME)

RN 148811-73-8 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-L-tryptophyl-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 148811-74-9 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-L-tryptophyl-, (S)- (9CI) (CA INDEX NAME)

RN 148811-75-0 HCAPLUS

CN L-Alaninamide, 4-chloro-N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-L-phenylalanyl-, (S)- (9CI) (CA INDEX NAME)

RN 148811-76-1 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-3-methoxy-0-methyl-L-tyrosyl-, (S)- (9CI) (CA INDEX NAME)

RN 148811-77-2 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-3-(1-naphthalenyl)-L-alanyl-N-methyl-, (S)- (9CI) (CA INDEX NAME)

RN 148811-78-3 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-1-methyl-2-oxoethyl]-4-methyl-1-oxopentyl]-L-phenylalanyl-, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

RN 148811-79-4 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-1-methyl-2-oxoethyl]-4-methyl-1-oxopentyl]-L-phenylalanyl-, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

RN 148811-80-7 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-1-methyl-2-oxoethyl]-4-methyl-1-oxopentyl]-L-phenylalanyl-, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

RN 148811-81-8 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-1-methyl-2-oxoethyl]-4-methyl-1-oxopentyl]-L-phenylalanyl-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

RN 148811-82-9 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-1-methyl-2-oxoethyl]-4-methyl-1-oxopentyl]-L-tryptophyl-, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

RN 148811-83-0 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-1-methyl-2-oxoethyl]-4-methyl-1-oxopentyl]-L-tryptophyl-, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

RN 148811-84-1 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-1-methyl-2-oxoethyl]-4-methyl-1-oxopentyl]-L-tryptophyl-, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

RN 148811-85-2 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-1-methyl-2-oxoethyl]-4-methyl-1-oxopentyl]-L-tryptophyl-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

RN 148811-86-3 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxymethylamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-L-phenylalanyl-, (S)- (9CI) (CA INDEX NAME)

1T 148745-00-0P 148745-09-9P 148811-56-7P 148811-66-9P 148811-67-0P 148811-68-1P

RL: SPN (Synthetic preparation); PREP (Preparation) (preparation and collagenase-inhibiting activity of)

RN 148745-00-0 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-3-(1-naphthalenyl)-L-alanyl-, (R)- (9CI) (CA INDEX NAME)

RN 148745-09-9 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-1-methyl-2-oxoethyl]-4-methyl-1-oxopentyl]-3-(1-naphthalenyl)-L-alanyl-, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

RN 148811-56-7 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-3-(1-naphthalenyl)-L-alanyl-, (S)- (9CI) (CA INDEX NAME)

RN 148811-66-9 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-1-methyl-2-oxoethyl]-4-methyl-1-oxopentyl]-3-(1-naphthalenyl)-L-alanyl-, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

RN 148811-67-0 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-1-methyl-2-oxoethyl]-4-methyl-1-oxopentyl]-3-(1-naphthalenyl)-L-alanyl-, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

RN 148811-68-1 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-1-methyl-2-oxoethyl]-4-methyl-1-oxopentyl]-3-(1-naphthalenyl)-L-alanyl-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

IT 148745-39-5P 148745-40-8P 148745-43-1P

148811-88-5P 148812-14-0P

RN 148745-39-5 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 148745-40-8 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-3-(3-pyridinyl)-L-alanyl- (9CI) (CA INDEX NAME)

RN 148745-43-1 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-3-(2-naphthalenyl)-L-alanyl-N-ethyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 148811-88-5 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-3-methoxy-0-methyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 148812-14-0 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-1-methyl-2-oxoethyl]-4-methyl-1-oxopentyl]-3-(1-naphthalenyl)-L-alanyl- (9CI) (CA INDEX NAME)

L20 ANSWER 56 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1993:829 HCAPLUS

DOCUMENT NUMBER:

118:829

TITLE:

Mammalian matrix metalloprotease inhibitors for

treatment of tissue ulceration

INVENTOR (S):

Galardy, Richard E.; Grobelny, Damian; Schultz,

Gregory

PATENT ASSIGNEE(S):

University of Florida, USA

SOURCE:

U.S., 13 pp. CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

I	PATEN'	r no.	•		KI	ND	DATE			A	PPLI	CATIO	ON NO	ο.	DATE			
Ţ	JS 51	14953	3	A		19920519			U.	 S 19	90-61	1602	 1	1990	1121			
	CA 20:	96223	3		A	A	19920522			C.	A 19	91-20	09622	23	1991	1121		
	CA 20																	
V	VO 92	09282	2		A	1 .	1992	0611		W	0 19	91-U	3872	1	1991	1121		
	W	: A7	C, 2	AU,	BB,	BG,	BR,	CA,	CH,	CS,	DE,	DK,	ES,	FI,	GB,	HU,	JP,	KP,
															SE,			
	R														FR,		GB,	GN,
							MR,						•	•	•	•	·	•
I	AU 91												1351		1991	1121		
I	AU 65:	2016			В.	2	1994	0811										
	EP 55									E	P 19	92-90	02666	5	1991	1121		
	EP 55																	
	R	: A	ľ, 1	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE		
-	JP 05																	
	JP 06	10262	26		В	4	1994	1214		J	P 19	91-50	0280	5	1991	1121		
I	AT 16	1767			Ε		1998	0415		A'	Т 19	92-90	02666	5	1991	1121		
E	ES 21	15668	3		T	3	1998	0701		E	S 19	92-90	02666	5	1991	1121		
Ţ	JS 52	70326	5		Α		1993	1214		U	S 19	92-88	31630)	1992	0512		
N	10 93	01803	3		Α		1993	0518		N	0 19	93-18	303		1993	0518		
ι	JS 58	92112	2		Α		1999	0406		U	S 19	94-18	3472	7	1994	0121		
	JS 57																	
PRIORI					. :				τ	JS 1	990-	4777	51	B2	1994 1990	0209		
		•							τ	JS 1	990-	61579	98	A2	1990	1121		
									Ţ	JS 1	990-	61602	21	Α	1990	1121		
															1991			
										TO 1	001			3.0	1991	0000		

WO 1991-US8721 A 19911121 US 1992-817039 A2 19920107 US 1992-881630 A1 19920512 US 1993-44324 A2 19930407 US 1994-184727 A3 19940121

OTHER SOURCE(S):

MARPAT 118:829

Amethod to treat or prevent ulceration of tissue comprises administering an effective amount of a mammalian matrix metalloprotease inhibitor HONHCOCR1HCR2HCON(R3)CR4HCOX or HONHCOC(R1)=C(R2)CON(R3)C(R4)HCOX [R1 = H; R2 = C3-8 alkyl; or R1 and R2 together = (CH2)n; n = 3-5; R3 = H C1-4 alkyl; R4 = fused or conjugated (un)substituted bicycloaryl methylene; X = OR5, NHR5, amino acid residue, amide of amino acid residue, cyclic amine residue, heterocyclic amine residue; R5 = H, (un)substituted C1-12 alkyl, C6-12 aryl, C6-16 arylalkyl]. NHOHCOCH2CH(iso-Bu)CO-L-TrpNHMe (I) inhibited human skin fibroblast collagenase with a Ki = 10 nM. I prevented corneal ulceration in alkali-burned rabbit cornea.

IT 142880-58-8P 142880-59-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and reaction of, in ulcer inhibitor preparation)

RN 142880-58-8 HCAPLUS

CN Butanediamide, N1-[2-(dodecylamino)-1-(1H-indol-3-ylmethyl)-2-oxoethyl]-N4hydroxy-2-(2-methylpropyl)-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 142880-59-9 HCAPLUS

CN Butanediamide, N1-[2-(dodecylamino)-1-(1H-indol-3-ylmethyl)-2-oxoethyl]-N4hydroxy-2-(2-methylpropyl)-, monopotassium salt (9CI) (CA INDEX NAME)

K

Absolute stereochemistry.

RN 142880-37-3 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 142880-38-4 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1R)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

RN 142880-40-8 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-N1-methyl-2-(2-methylpropyl)- (9CI) (CA INDEX NAME)

RN 142880-46-4 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[2-[(2-hydroxyethyl)amino]-1-(1H-indol-3-ylmethyl)-2-oxoethyl]-2-(2-methylpropyl)- (9CI) (CA INDEX NAME)

RN 142880-50-0 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[1-(1H-indol-3-ylmethyl)-2-oxo-2-(pentylamino)ethyl]-2-(2-methylpropyl)-, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

RN 142880-53-3 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[1-(1H-indol-3-ylmethyl)-2-oxo-2-(pentylamino)ethyl]-2-(2-methylpropyl)-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 142880-57-7 HCAPLUS

CN Butanediamide, N1-[2-(dodecylamino)-1-(1H-indol-3-ylmethyl)-2-oxoethyl]-N4-hydroxy-2-(2-methylpropyl)-, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 142880-60-2 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[1-(1H-indol-3-ylmethyl)-2-oxo-2-[(1-phenylethyl)amino]ethyl]-2-(2-methylpropyl)- (9CI) (CA INDEX NAME)

RN 142880-62-4 HCAPLUS

CN Carbamic acid, [6-[[(2S)-2-[[(2S)-2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]amino]-3-(1H-indol-3-yl)-1-oxopropyl]amino]hexyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 142880-75-9 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1R)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 142902-71-4 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)- (9CI) (CA INDEX NAME)

L20 ANSWER 57 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1992:651774 HCAPLUS

DOCUMENT NUMBER:

117:251774

TITLE:

Preparation of substituted amino acids as matrix

metalloprotease inhibitors

INVENTOR (S):

Galardy, Richard E.; Grobelny, Damian

PATENT ASSIGNEE(S):

USA

SOURCE:

PCT Int. Appl., 58 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.				KIND DATE			APPLICATION NO. DATE										
WO	92095	556		A	 1	 1992	0611		W	0 19	91-U	3872	3	1991	1121		
	W:	AT,	AU,	BB,	BG,	BR,	CA,	CH,	CS,	DE,	DK,	ES,	FI,	GB,	HU,	JP,	ΚP,
		KR,	LK,	LU,	MC,	MG,	MN,	MW,	NL,	NO,	PL,	RO,	SD,	SE,	SU		
	RW:	ΑT,	ΒĒ,	BF,	ВJ,	CF,	CG,	CH,	CI,	CM,	DE,	DK,	ES,	FR,	GA,	GB,	GN,
		GR,	IT,	LU,	ML,	MR,	∙NL,	SE,	SN,	TD,	TG						
	51839																
	51891																
	20962																
AU	91909	958		A	1	1992	0625		A	U 19	91-90	0958		1991	1121		
AU	66250)4		B	2	1995	0907										
EP	55864	18		A	1	1993	0908		E	P 19	92-90	01322	2	1991	1121		
	R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE		
JP	05508	3163		T	2	1993	1118		J	P 19	92-50	01548	В	1991	1121		
JP	27362	285		B:	2	1998	0402		J	P 19	91-50	01548	В	1991	1121		
NO	93018	341		Α		1993	0519		N	0 19	93-18	841		1993	0519		
PRIORITY	Y APPI	IN.	INFO	. :				τ	JS 1	990-	61579	98	Α	1990	1121		
								Ţ	JS 1	991-	74775	52	Α	1991	0820		
								1	NO 1	991-1	US872	23	Α	1991	1121		

OTHER SOURCE(S): MARPAT 117:251774

AB Title compds. R7ONR6CO(CHR1)nCHR2CONR3CHR4COX and

R7ONR6CO(CHR1)mCR1:CR2CONR3CHR4COX [R1 = H, C1-8 alkyl; R2 = C1-8; or R1R2 = (CH2)p wherein p = 3-5; R3, R6 = H, C1-4 alkyl; R4 = fused or conjugated (substituted) bicycloarylmethylene; n = 0-2; m = 0, 1; X = R5O, R5NH wherein R5 = H, (substituted) C1-12 alkyl, C6-12 aryl, C6-16 alkylaryl, amino acid, amide, cyclic amine heterocyclic amine; R7 = H, C1-4 alkyl, acyl, and wherein CONR3 is optionally in modified isosteric form], are

prepared To a mixture of MeO2CCH2CH(CH2CHMe2)CO2H (preparation given) and (COC1)2

in CH2Cl2 was added DMT at room temperature to give an intermediate to which was

added L-tryptophan (S)-methylbenzylamide to give after workup

 $\label{thm:hondood} \begin{tabular}{ll} HONHCOCH2CH (Me2CHCH2)CO-L-Trp-NH-(S)-CHMePhe (I). & I inhibited \\ metalloprotease with Ki of 3 mM. \end{tabular}$

IT 143985-51-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and neutralization of)

RN 143985-51-7 HCAPLUS

CN Butanediamide, N1-[2-(dodecylamino)-1-(1H-indol-3-ylmethyl)-2-oxoethyl]-N4-hydroxy-2-(2-methylpropyl)-, monopotassium salt, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

• K

Absolute stereochemistry.

RN 142880-37-3 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-

2-oxoethyl]-2-(2-methylpropyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 142880-38-4 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1R)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 142880-53-3 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[1-(1H-indol-3-ylmethyl)-2-oxo-2-(pentylamino)ethyl]-2-(2-methylpropyl)-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 142880-58-8 HCAPLUS

CN Butanediamide, N1-[2-(dodecylamino)-1-(1H-indol-3-ylmethyl)-2-oxoethyl]-N4-hydroxy-2-(2-methylpropyl)-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 142880-60-2 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[1-(1H-indol-3-ylmethyl)-2-oxo-2-[(1-phenylethyl)amino]ethyl]-2-(2-methylpropyl)- (9CI) (CA INDEX NAME)

RN 142880-62-4 HCAPLUS

CN Carbamic acid, [6-[[(2S)-2-[[(2S)-2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]amino]-3-(1H-indol-3-yl)-1-oxopropyl]amino]hexyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 142880-75-9 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1R)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-, (2S)- (9CI) (CA INDEX NAME)

RN 143985-20-0 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-N1-methyl-2-(2-methylpropyl)-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 143985-22-2 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[2-[(2-hydroxyethyl)amino]-1-(1H-indol-3-ylmethyl)-2-oxoethyl]-2-(2-methylpropyl)-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 143985-24-4 HCAPLUS

CN Butanediamide, N4-(acetyloxy)-N1-[1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

RN 143985-25-5 HCAPLUS

CN Butanediamide, N4-(benzoyloxy)-N1-[1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 144007-85-2 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-N4-methyl-2-(2-methylpropyl)- (9CI) (CA INDEX NAME)

RN 144007-86-3 HCAPLUS

CN Butanediamide, N4-ethyl-N4-hydroxy-N1-[1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)- (9CI) (CA INDEX NAME)

RN 144007-87-4 HCAPLUS

CN Butanediamide, N4-(benzoyloxy)-N1-[1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)- (9CI) (CA INDEX NAME)

RN 144007-88-5 HCAPLUS

CN Butanediamide, N4-(acetyloxy)-N1-[1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-N4-methyl-2-(2-methylpropyl)- (9CI) (CA INDEX NAME)

RN 144007-89-6 HCAPLUS

CN Butanediamide, N4-(benzoyloxy)-N4-ethyl-N1-[1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)- (9CI) (CA INDEX NAME)

RN 144022-77-5 HCAPLUS

CN Butanediamide, N1-[2-(ethylamino)-1-(1H-indol-3-ylmethyl)-2-oxoethyl]-N4-methoxy-2-(2-methylpropyl)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & & & \\ H & & & & & \\ N & & & & \\ NH-C-CH-Bu-i \\ & & & \\ CH_2-CH-C-NHEt \\ & & & \\ 0 & & \\ \end{array}$$

RN 144022-78-6 HCAPLUS

CN Butanediamide, N4-ethoxy-N1-[2-(ethylamino)-1-(1H-indol-3-ylmethyl)-2-oxoethyl]-N4-methyl-2-(2-methylpropyl)- (9CI) (CA INDEX NAME)

RN 144069-98-7 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[1-(1H-indol-3-ylmethyl)-2-oxo-2-[(1-phenylethyl)amino]ethyl]-2-(2-methylpropyl)-, [2S-[N1[R*(R*)],2R*]]- (9CI) (CA INDEX NAME)

L20 ANSWER 58 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1992:612958 HCAPLUS

DOCUMENT NUMBER:

117:212958

TITLE:

Preparation of substituted amino acids as matrix

metalloprotease inhibitors

INVENTOR(S):

Galardy, Richard E.; Grobelny, Damian; Musser, John H. Glycomed, Inc., USA

PATENT ASSIGNEE(S):

PCT Int. Appl., 64 pp.

SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.						APPLICATION NO.						DATE						
Ĭ	 WO	9209													1991	1121		
		W:	ΑT,	AU,	BB,	BG,	BR,	CA,	CH,	CS,	DE,	DK,	ES,	FI,	GB,	HU,	JP,	KΡ,
			KR,	LK,	LU,	MC,	MG,	MN,	MW,	NL,	NO,	PL,	RO,	SD,	SE,	SU		
		RW:	ΑT,	BE,	BF,	ВJ,	CF,	CG,	CH,	CI,	CM,	DE,	DK,	ES,	FR,	GA,	GB,	GN,
			GR,	IT,	LU,	ML,	MR,	ΝL,	SE,	SN,	TD,	TG						
1	US	5183	900		Α		1993	0202		U	S 19	90-6	1579	В	1990	1121		
1	US	5239	078		Α		1993	0824		U	S 19	91-7	4775	1.	1991	0820		
		9190								A	J 19	91-9	0897		1991	1121		
1	AU	6612	89		B	2	1995	0720										,
		2096																
]	EP	5586	35		A	1	1993	0908		Ε	P 19	92-9	0111	9	1991	1121		
]	ΕP	5586	35		В	1	1997	0910										
				-					-	-		-			ΝL,			
		0708																
		1579																
		2109													1991			
		9301													1993			
PRIOR	ITY	APP	LN.	INFO	.:													
															1991			
															1991			
											991-	US87:	22	Α	1991	1121		
THER	SC	URCE	(S):			MAR	PAT	117:2	2129	58								

Title compds. Y(CHR1)nCHR2CONR3CHR4COX and Y(CHR2)mCR1:CR2CONR3CHR4COX (R1 = H, C1-8 alkyl; R2 = C1-8 alkyl; or R1R2 = (CH2)p wherein p = 3-5; R3 =H, C1-4 alkyl; R4 = (substituted) fused or conjugated bicycloarylmethylene; n = 0-2; m = 0, 1; X = R50, R5NH wherein R5 = H, (substituted) C1-12alkyl, C6-12 aryl, C6-16 arylalkyl, amino or amide residue, cyclic amine or heterocyclyl; Y = R70NR6CONR6, (R6)2NCONOR7, R6CONOR7 wherein R6 = H, C1-4 alkyl; R7 = C1-4 alkyl, acyl; CONR3 is optionally in modified

isosteric form], are prepared. To a mixture of MeO2CCH2CH(CH2CHMe2)CO2H (preparation given) and (COCl)2 in CH2Cl2, anhydrous DMF was added, and to the residue obtained was added L-tryptophan (S)-methylbenzylamide to give NHOHCOCH2CH(CH2CHMe)2CO-L-Trp-NH-(S)-CHMePh (I). I inhibited metalloprotease with Ki of 3 μM .

IT 143985-51-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and neutralization of)

RN 143985-51-7 HCAPLUS

CN Butanediamide, N1-[2-(dodecylamino)-1-(1H-indol-3-ylmethyl)-2-oxoethyl]-N4-hydroxy-2-(2-methylpropyl)-, monopotassium salt, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

● K

Absolute stereochemistry.

RN 142880-37-3 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1S)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-

2-oxoethyl]-2-(2-methylpropyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 142880-38-4 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1R)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 142880-53-3 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[1-(1H-indol-3-ylmethyl)-2-oxo-2-(pentylamino)ethyl]-2-(2-methylpropyl)-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 142880-58-8 HCAPLUS

CN Butanediamide, N1-[2-(dodecylamino)-1-(1H-indol-3-ylmethyl)-2-oxoethyl]-N4-hydroxy-2-(2-methylpropyl)-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 142880-62-4 HCAPLUS

CN Carbamic acid, [6-[[(2S)-2-[[(2S)-2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]amino]-3-(1H-indol-3-yl)-1-oxopropyl]amino]hexyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 142880-75-9 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[(1R)-1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 143985-20-0 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-N1-methyl-2-(2-methylpropyl)-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

RN 143985-22-2 HCAPLUS

CN Butanediamide, N4-hydroxy-N1-[2-[(2-hydroxyethyl)amino]-1-(1H-indol-3-ylmethyl)-2-oxoethyl]-2-(2-methylpropyl)-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 143985-24-4 HCAPLUS

CN Butanediamide, N4-(acetyloxy)-N1-[1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 143985-25-5 HCAPLUS

CN Butanediamide, N4-(benzoyloxy)-N1-[1-(1H-indol-3-ylmethyl)-2-(methylamino)-2-oxoethyl]-2-(2-methylpropyl)-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

144069-98-7 HCAPLUS RN

Butanediamide, N4-hydroxy-N1-[1-(1H-indol-3-ylmethyl)-2-oxo-2-[(1-CNphenylethyl) amino] ethyl] -2 - (2 - methylpropyl) -, [2S - [N1[R*(R*)], 2R*]] - (9CI)(CA INDEX NAME)

Absolute stereochemistry.

HCAPLUS COPYRIGHT 2004 ACS on STN L20 ANSWER 59 OF 63

ACCESSION NUMBER:

1991:559788 HCAPLUS

DOCUMENT NUMBER:

115:159788

TITLE:

Preparation of (hydroxyamino) amino acids as

collagenase inhibitors

INVENTOR(S):

Campion, Colin; Davidson, Alan Hornsby; Dickens,

Jonathan Philip; Crimmin, Michael John

PATENT ASSIGNEE(S):

British Bio-Technology Ltd., UK PCT Int. Appl., 70 pp.

SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND DATE	APPLICATION NO. DATE
-		
WO 9102716	A2 19910307	WO 1990-GB1117 19900720
WO 9102716	A3 19910627	
W: AU, CA	, FI, JP, KR, NO,	US
RW: AT, BE	, CH, DE, DK, ES,	FR, GB, IT, LU, NL, SE
CA 2064786	AA 19910225	CA 1990-2064786 19900720
AU 9060454	A1 19910403	AU 1990-60454 19900720
AU 639706	B2 19930805	

EP	489032	}	A1	19920610		EP 1990-911398	19900720
EP	489032	!	B1	19940914			
	R: A	T, BE,	CH, D	E, DK, ES,	FR, GE	B, IT, LI, LU, N	L, SE
JP	055018	864	T2	19930408		JP 1990-510523	19900720
JP	287184	9	B2	19990317			
ES	206397	15	Т3	19950116		ES 1990-911398	19900720
US	545343	8	Α	19950926	•	US 1992-820664	19920116
NO	920070	2	Α	19920423		NO 1992-702	19920221
US	591060	9	Α	19990608		US 1995-417095	19950405
PRIORITY	Y APPLN	I. INFO).:		GB	1989-19251	19890824
					WO	1990-GB1117	19900720
OTHER SO	OURCE (S	5):	M	ARPAT 115:	159788		

AB Title compds. HONHCOCHR1CHR2CONHCHR3CONR4R5 [I; R1 = H, C1-6 alkyl, C1-6 alkenyl, phenyl-C1-6 alkylthiomethyl, (substituted) phenylthiomethyl, heterocyclthiomethyl, etc.; R2 = H, C1-6 alkyl, C1-6 alkenyl, cycloalkyl-C1-6-alkyl, etc.; R3 = amino acid side chain, C1-6 alkyl, PhCH2, PhCH2OPhCH2, etc.; R4 = H, Me; R5 = hydroxyalkyl, C1-6 alkoxyalkyl, phenylthioalkyl, C2-7 acylaminoalkyl, etc.; R4R5N = hydroxymethyl-, carboxyheterocyclyl], salt, N-oxide, sulfoxide, sulfone thereof, are prepared I are useful in promotion of wound healing (no data). [4-(4-Benzyloxyamino-2R-isobutylsuccinyl]-L-phenylalanine (preparation given) was coupled with EtSCH2CH2NH2.HCl, and the product hydrogenated to give the amide II. In test for collagenase inhibition activity II showed an IC50 of 20 μM. Pharmaceutical formulations comprising I are given.
IT 135775-00-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation of, as collagenase inhibitor)

RN 135775-00-7 HCAPLUS

CN Butanediamide, N1-[2-[[2-(acetylamino)ethyl]amino]-2-oxo-1-(phenylmethyl)ethyl]-N4-hydroxy-2-(2-methylpropyl)-, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

L20 ANSWER 60 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1990:590468 HCAPLUS

DOCUMENT NUMBER: 113:190468

TITLE: Preparation and formulation of hydroxamic acid

derivatives as collagenase inhibitors

INVENTOR(S): Davidson, Alan Hornsby; Dickens, Jonathan Philip;

Crimmin, Michael John

PATENT ASSIGNEE(S): British Bio-Technology Ltd., UK

SOURCE: PCT Int. Appl., 105 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PAT	ENT NO.		KIND	DATE	APPLICATION NO. DATE
WO				19900531 , NO, US	WO 1989-GB1398 19891123
	•	,	•		GB, IT, LU, NL, SE
CA					CA 1989-2003719 19891123
					AU 1990-47468 19891123
				19930930	
					EP 1990-900268 19891123
				19940316	
					GB, IT, LI, LU, NL, SE
					JP 1990-500815 19891123
AT	102919		E	19940415	AT 1990-900268 19891123
					ES 1990-900268 19891123
	2846737				JP 1989-500815 19891123
US	5304604		Α	19940419	US 1991-674363 19910415
					DK 1991-967 19910522
NO	9101963				NO 1991-1963 19910522
				19950731	
NO	177700		С	19951108	
				19960507	US 1994-229154 19940418
	APPLN.				GB 1988-27308 19881123
•					EP 1990-900268 19891123
					WO 1989-GB1398 19891123
					US 1991-674363 19910415
OTHER SO	OURCE(S):		CA	SREACT 11	3:190468; MARPAT 113:190468

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Hydroxamic acid derivs. [I; R1 = H, C1-6 alkyl, alkenyl, Ph, OS, etc.; R2 = H, C1-6 alkyl, alkenyl, phenylalkyl, etc.; R1 = amino acid residue, C2-6 alkyl, PhCH2, etc.; R4 = H, Me; n = 1-6; A = NH2, substituted acyclic amino, heterocycle residue, etc.], their N-oxides, sulfoxides, or sulfones, having collagenase inhibitory activity useful in treating arthropathy, inflammation, dematolog. diseases, bone resorption diseases, and tumor invasion (no data), are prepared and formulated. Saponification of Me

ester (2R)-L-II (R = Me) with LiOH in MeOH gave 71% and (2R)-L-II (R = H), which was dissolved in THF and treated with pyrrolidine derivative III, Et3N,

and ClCO2Et to give 72% (2R,2'RS)-L-IV. Also prepared were 38 addnl. I which showed collagenase inhibitory activity with IC50 = 15-70 nM. Tablet, capsule, injection, suppository, and ointment formulations were given.

130128-39-1P IT

RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of, as collagenase inhibitor)

130128-39-1 HCAPLUS RN

Butanediamide, N1-[2-[[2-(diethylamino)ethyl]amino]-2-oxo-1-CN(phenylmethyl)ethyl]-N4-hydroxy-3-methyl-2-(2-methylpropyl)-, [2R-[1(S*),2R*,3S*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$\begin{array}{c|c} \text{Et}_2 \text{N} & \begin{array}{c} \text{O} \\ \text{N} \\ \text{H} \end{array} & \begin{array}{c} \text{H} \\ \text{S} \\ \text{N} \end{array} & \begin{array}{c} \text{O} \\ \text{N} \\ \text{H} \end{array} & \begin{array}{c} \text{OH} \\ \text{Me} \end{array}$$

L20 ANSWER 61 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1989:412332 HCAPLUS

DOCUMENT NUMBER:

111:12332

TITLE:

Hair tonics containing proteoglycanase inhibitors,

glycosaminoglycanase inhibitors, and inhibitors of

cellular uptake of glycosaminoglycans

PATENT ASSIGNEE(S):

SOURCE:

Unilever N. V., Neth.

Jpn. Kokai Tokkyo Koho, 38 pp.

CODEN: JKXXAF

DOCUMENT TYPE:

LANGUAGE:

Patent Japanese

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 63166823	Δ2	19880711	JP 1987-326597	19871223
	B4	19910425	01 230, 02003,	
	A1	19930706	CA 1987-554275	19871214
US 5015470	A	19910514	US 1987-134422	19871217
AU 8782813	A1	19880623	AU 1987-82813	19871218
AU 615170	B2	19910926		
ZA 8709564	Α	19890830	ZA 1987-9564	19871221
IN 166979	A	19900811	IN 1987-BO370	19871221
EP 277428	A2	19880810	EP 1987-311315	19871222
EP 277428	A3	19910313		
EP 277428	B1	19940323		
	•		GR, IT, LI, NL, SE	
AT 103165	. E	19940415	AT 1987-311315	19871222
ES 2051758	Т3	19940701	ES 1987-311315	19871222
BR 8707033	Α	19880802	BR 1987-7033	19871223
PRIORITY APPLN. INFO	.:	GI	B 1986-30721	19861223
		El	P 1987-311315	19871222

Hair tonics are prepared which contain enzyme inhibitors, such as AB

proteoglycanase inhibitors, glycosaminoglycanase inhibitors, and inhibitors of cell uptake of glycosaminoglycans, and vehicles as carriers of these inhibitors. Thus, a hair lotion was prepared consisting of L-galactono-1,4-lactone 0.1, EtOH 99.995% by weight and a perfume q.s. Thirty other hair lotions and tonics were prepared

IT 106314-87-8

RL: BIOL (Biological study)

(proteoglycanase inhibitor, hair tonic containing)

RN 106314-87-8 HCAPLUS

CN L-Phenylalaninamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L20 ANSWER 62 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

Patent

ACCESSION NUMBER:

1988:167973 HCAPLUS

DOCUMENT NUMBER:

108:167973

TITLE:

Preparation of (hydroxylamino)acylpeptides as

inhibitors of synovial collagenase

INVENTOR(S):

Handa, Balraj Krishnan; Johnson, William Henry;

Machin, Peter James

PATENT ASSIGNEE(S):

Hoffmann-La Roche, F., und Co. A.-G., Switz.

SOURCE:

Eur. Pat. Appl., 24 pp. CODEN: EPXXDW

DOCUMENT TYPE:

LANGUAGE: German

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 236872	A2	19870916	EP 1987-102771	19870226
EP 236872	A3	19890913		
EP 236872	B1	19921125		
R: AT, BE,	CH, DE	, FR, GB, IT,	LI, LU, NL, SE	
DK 8700774	Α	19870912	DK 1987-774	19870216
AT 82753	E	19921215	AT 1987-102771	19870226
CA 1314655	A1	19930316	CA 1987-530988	19870303
ZA 8701563	Α	19871028	ZA 1987-1563	19870304
IL 81790	A1	19910310	IL 1987-81790	19870305
AU 8769902	A 1	19870917	AU 1987-69902	19870311
AU 588437	B2	19890914		
JP 62230757	A2	19871009	JP 1987-56412	19870311
JP 06029228	B4	19940420		
US 4996358	Α	19910226	US 1989-336264	19890411
PRIORITY APPLN. INFO.	:	G	B 1986-5977	19860311
		· G	B 1986-29712	19861212
		U	S 1987-14957	19870217

EP 1987-102771 19870226

AB ACHR3CHR1CONHCHR2CONR6CHR4R5 [I; A = HN(OH)CO, HCON(OH); R1 = alkyl; R2 = side chain of naturally-occurring amino acid, not H, Me; R2R4 = (CH2)n; R3 = H, amino, OH, SH, alkyl, alkoxy, alkylthio, arylalkyl, etc.; R4, R6 = H, Me; R5 = H, R4R5 = (CH2)3; alkyl, alkoxyalkyl, dialkoxymethylene, carboxy, acyl, carbamoyl; n = 4-11] and pharm. acceptable salts were prepared for treatment of degenerative joint disease. [2(R)-Isobutylsuccinyl]-L-leucyl-L-alanine Et ester (preparation given) in THF at -15° was treated with iso-Bu chloroformate and N-ethylmorpholine followed by O-benzylhydroxylamine. The resulting benzyloxyamino derivative was hydrogenoylzed in EtOH over 5% Pd/C to give 4-N-hydroxylaminol-2(R)-isobutylsuccinyl]-L-leucyl-L-alanine Et ester. The latter inhibited human synovial collagenase with an IC50 of 8.5 + 10-9 M.

IT 112105-86-9P 112105-87-0P 112105-88-1P 112105-89-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and debenzylation of, in preparation of collagenase inhibitor)

RN 112105-86-9 HCAPLUS

CN Glycinamide, N-[4-methyl-1-oxo-2-[2-oxo-2-[(phenylmethoxy)amino]ethyl]pent yl]-L-leucyl-N-(3-methylbutyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 112105-87-0 HCAPLUS

CN Glycinamide, N-[4-methyl-1-oxo-2-[2-oxo-2-[(phenylmethoxy)amino]ethyl]pent yl]-L-valyl-N-ethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 112105-88-1 HCAPLUS

CN Glycinamide, N-[4-methyl-1-oxo-2-[2-oxo-2-[(phenylmethoxy)amino]ethyl]pent yl]-L-leucyl-N-ethyl- (9CI) (CA INDEX NAME)

112105-89-2 HCAPLUS RN

Glycinamide, N6-[(1,1-dimethylethoxy)carbonyl]-N2-[4-methyl-1-oxo-2-[2-oxo-CN 2-[(phenylmethoxy)amino]ethyl]pentyl]-L-lysyl-N-ethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

112105-58-5P 112105-59-6P 112105-60-9P ΙT

112105-61-0P 112105-63-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation of, as collagenase inhibitor)

RN112105-58-5 HCAPLUS

Glycinamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-Lleucyl-N-(3-methylbutyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN112105-59-6 HCAPLUS

Glycinamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-L-CN valyl-N-ethyl- (9CI) (CA INDEX NAME)

RN 112105-60-9 HCAPLUS

CN Glycinamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-L-leucyl-N-ethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 112105-61-0 HCAPLUS

CN Glycinamide, N6-[(1,1-dimethylethoxy)carbonyl]-N2-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-L-lysyl-N-ethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 112105-63-2 HCAPLUS

CN Glycinamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-0-methyl-L-tyrosyl-N-ethyl- (9CI) (CA INDEX NAME)

L20 ANSWER 63 OF 63 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1988:150980 HCAPLUS

DOCUMENT NUMBER:

108:150980

TITLE:

Preparation of hydroxyamino peptides as

metalloprotease inhibitors

INVENTOR(S):

Shaw, Andrew; Wolanin, Donald John

PATENT ASSIGNEE(S): SOURCE:

ICI Americas, Inc., USA Eur. Pat. Appl., 12 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 231081	A2	19870805	EP 1987-300366	19870116
EP 231081	A3	19891115		
EP 231081	B1	19930317		
R: AT, BE,	CH, DE	, ES, FR, GB,	GR, IT, LI, LU, NL	, SE
US 4771038	Α	19880913	US 1987-2814	19870113
AT 87005	E	19930415	AT 1987-300366	19870116
ES 2053525	Т3	19940801	ES 1987-300366	19870116
JP 62228097	A2	19871006	JP 1987-9207	19870120
JP 2532859	B2	19960911		
PRIORITY APPLN. INFO	· . :	(GB 1986-1368	19860121
		I	EP 1987-300366	19870116

AB HONHCO(CH2)n CHR1CONHCHR2CONHCHR3CONHA (I; R1 = alkyl; R2, R3, R4 = amino acid residue; A = H, CHR4CONH2; n = 1, 2) and pharmaceutically acceptable salts and maleate esters were prepared as metalloprotease inhibitors (no data). O-Benzylhydroxylamine was added to dihydro-3-pentyl-2,5-furandione in THF at -20° and the mixture was stirred 1 h at -20° to give 2-[2-oxo-2-(phenylmethoxyamino)ethyl]heptanoic acid. The latter in THF was treated with N-methylmorpholine and EtO2CCl at -15° for 1 h and coupled with H-Leu-Phe-NH2 in Me2SO at room temperature overnight. The product was debenzylated in MeOH over Pd/C to give I (R1 = pentyl, R2 = CH2CHMe2, R3 = CH2Ph, A = H, n = 1).

IT 113614-66-7P 113614-71-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and hydrogenolysis of)

RN 113614-66-7 HCAPLUS

CN L-Phenylalaninamide, N-[4-methyl-1-oxo-2-[2-oxo-2-

[(phenylmethoxy)amino]ethyl]pentyl]-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 113614-71-4 HCAPLUS

CN L-Leucinamide, N-[4-methyl-1-oxo-2-[2-oxo-2-[(phenylmethoxy)amino]ethyl]pentyl]-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT 106314-87-8P 113614-62-3P 113614-70-3P

RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of, as metalloprotease inhibitor)

RN 106314-87-8 HCAPLUS

CN L-Phenylalaninamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 113614-62-3 HCAPLUS

CN L-Alaninamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-L-valyl- (9CI) (CA INDEX NAME)

RN 113614-70-3 HCAPLUS

CN L-Leucinamide, N-[2-[2-(hydroxyamino)-2-oxoethyl]-4-methyl-1-oxopentyl]-L-leucyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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